EYE MOVEMENTS IN POSTERIOR FOSSA DISORDERS

An electro-oculographic study

Carsten Wennmo

Lund 1982

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Abstract

A quantitative analysis was made of smooth pursuit, voluntary saccades, and slow and fast phases of vestibular, optokinetic and optovestibular nystagmus in patients with disorders in the posterior fossa.

Patients with pontine disorders and combined cerebello-brainstem disorders had reduced velocities in smooth pursuit and voluntary saccades and frequently also in most types of slow and fast phases of nystagmus. Smooth pursuit and voluntary saccades seem to be more vulnerable than slow and fast phases of nystagmus.

Patients with medullary disorders had reduced smooth pursuit velocity but are distinguished from the previous groups by in some cases normal saccadic velocity and more frequently normal or even enhanced velocities in various types of nystagmus.

Patients with cerebellar disease had more often normal smooth pursuit and saccadic velocity and the velocities in the slow and fast phases of nystagmus were more frequently enhanced than in any other of the examined locations.

When the same eye-motor test battery was applied to patients diagnosed as suffering from vestibular neuronitis, 12 of 30 patients showed some evidence of possible involvement of the central nervous system.

An analysis of eye movements, with special reference to the velocities in different types of eye movements, may help to localize a disorder in the posterior fossa.

Key words
Brainstem, cerebellum, vestibular neuronitis, medulla oblongata, voluntary saccades, smooth pursuit, slow and fast phases of nystagmus.

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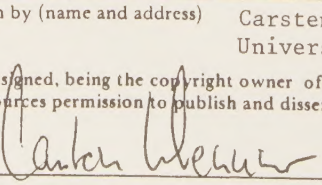
Signature 

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Lund 1982

The thesis is based on the following papers which will be referred to in the text by Roman numerals.

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II. Wennmo, C., Henriksson, N.G., Pyykkö, I. & Schalén, L. Eye-velocity programming in brainstem disorders.
Annals of the New York Academy of Sciences.
In press.

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IV. Wennmo, C. & Pyykkö, I. Vestibular neuronitis. A clinical and electro-oculographic study.
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Introduction

Vertigo is a sensation of disequilibrium frequently associated with inadequate control of balance. Among patients with vertigo, abnormal nystagmus, whether spontaneous or provoked by changes in gaze or position, can often be observed.

Traditionally, in diagnostic work-up, the site or origin of the disorder has been looked for by examining vestibulo-ocular and optokinetic reflexes. In the analysis of these responses much attention has been focused on the slow phases of nystagmus (2, 65, 77, 117).

However, as early as 1903 Dodge (49) described the four basically different types of conjugate eye movements which can be examined separately in humans. Studies of oculomotor abnormalities in various disorders causing vertigo have shown that analysis of these different types of eye movements, i.e. slow and fast phases of nystagmus, saccades and smooth pursuit, may supply important information about the pathophysiology of vertigo and dizziness (9, 54)*.

Each of the four types of eye movements presented above can be analyzed and described by means of different parameters (9, 21, 54), not all of which are

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* The smooth pursuit is an eye movement that holds an object in the fovea during movement of the target. The voluntary saccades consist of rapid refixational eye movements that bring a new part of the visual field to the fovea. During rotation in light and during optokinetic stimulus the slow phase allows a constant fixation on the fovea while the fast phase rapidly moves the fovea to a new target.

as yet well established, and different laboratories may well use different methods of analysis and description. In the present study the main interest is focused on the velocity of the various eye movements, since the velocity parameter has been found informative in examining patients with posterior fossa disorders (10, 13, 133, 135).

ANATOMY AND PHYSIOLOGY OF OCULOMOTOR MECHANISMS

For obvious reasons, the mechanisms involved in oculomotor control are not as well documented in humans as in animals, and experimental data is the main basis for interpretation of defective eye movements in humans. Therefore some important observations on oculomotor control in animals are presented below.

Brainstem

The vestibulo-ocular reflex arc consists of the peripheral labyrinth, the vestibular nerve, the vestibular nuclei and the oculomotor nuclei (86, 119). Impulses from the peripheral labyrinth are conveyed via a three-neuron reflex arc to the oculomotor nuclei (120). With Lorente de Nó's observation (86) that transection of the medial longitudinal fasciculus does not prevent vestibulo-ocular responses, it became evident that the brainstem outside the classical three-neuron reflex arc is involved in generation of vestibulo-ocular responses. This concept of the vestibular system has been extended to the paramedian pontine reticular formation, the inferior olive and the nucleus prepositus hypoglossi (Fig. 1).

The function of the labyrinths and the vestibular nuclei is important for the performance of normal vestibular nystagmus as well as for optokinetic

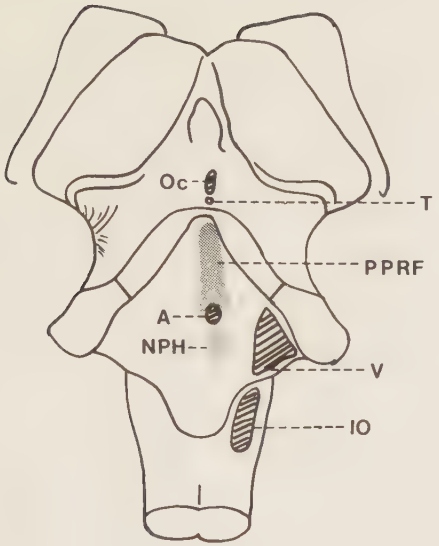
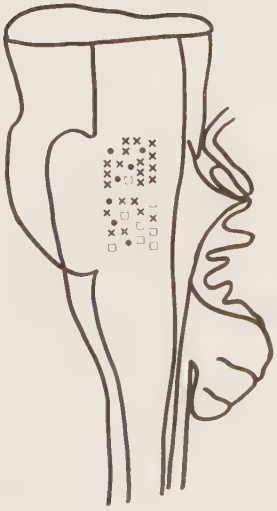


Fig. 1. A schematic diagram of the brainstem. Oc = oculomotor nucleus. T = trochlear nucleus. PPRF = paramedian pontine reticular formation. A = abducens nucleus. NPH = nucleus prepositus hypoglossi. V = vestibular nucleus. IO = inferior olive.

Fig. 2. Hypothetic locations of various kinds of eye motor neurons according to Luschei & Fuchs (87). ✕ = burst units. □ = tonic units. ● = pausing units.



nystagmus (1, 44, 64, 102).

The velocity encoding of smooth pursuit, voluntary saccades and slow and fast phases of nystagmus takes place in the brainstem, particularly in the paramedian pontine reticular formation (78, 87). The neurons for velocity encoding of rapid eye movements, burst units, are located more rostrally in pons (78, 87, 115) than units for slow eye movements, tonic units (Fig. 2). Because of this, lesions in the upper pons may have a more severe effect on saccades and fast phases of nystagmus than a lesion in the lower pons.

Neurons within the medulla oblongata, more specifically the inferior olive (89), and the nucleus prepositus hypoglossi (7), convey important information associated with eye movements. The inferior olive seems to relay visual information projected to the cerebellar flocculus (90) and both floccular and olivary lesions can have a detrimental effect on visually evoked eye movements (24, 73, 134). Therefore it may be difficult to separate cerebellar and medullary disorders by analyzing eye movements.

The above-mentioned brainstem structures are described below in greater detail.

The vestibular nuclei

The vestibular nuclei are located laterally below the floor of the caudal half of the fourth ventricle, partly in the pons and partly in the medulla oblongata (Fig. 1). These nuclei relay signals from the peripheral labyrinths, with additional processing of vestibular and visual signals (126, 127). Thus, during optokinetic stimulation, a discharge of neuronal activity has been observed in the vestibular nuclei in animals (1, 64). Further, lesions of the vestibular nuclei (4, 124) and the labyrinths (44, 59) may impair vestibular and optokinetic nystagmus. While the majority of impulses from the vestibular nuclei reach the oculomotor nuclei via the medial longitudinal fasciculus, others are conveyed via multisynaptic pathways through the paramedian pontine reticular formation or via the cerebellum (37, 86).

The paramedian pontine reticular formation

The paramedian pontine reticular formation (PPRF) is located in the medial pons between the trochlear and abducens nucleus (Fig. 1). The PPRF receives pathways from cerebral and cerebellar areas and from the vestibular nuclei (36, 57) and also projects directly to the oculomotor nuclei (36, 57). The PPRF is regarded as an important centre for oculomotor integration (104) as destruction of this area causes paralysis of ipsilateral conjugate gaze (25, 42, 56). Furthermore, recordings in monkeys indicate that saccades and fast phases of nystagmus in the horizontal plane are generated in the PPRF (40, 41, 87). The pontine reticular formation contains neuronal units which may be divided into four general categories (78, 87). Burst units, mainly located in the rostral part of the PPRF, discharge before and during rapid eye movements (Fig. 2). The same type of activity is found no matter whether the rapid eye movements are visually or vestibularly evoked. Tonic units, located more caudally in the periabducens region, discharge in relation to eye position (Fig. 2). Pausing units, scattered irregularly in the reticular formation, discharge during fixation and slow eye movements, and the activity decreases during rapid eye movements (Fig. 2). Burst-tonic units, scattered around the abducens nucleus, discharge during saccades and maintain a tonic activity related to steady eye position. Investigators have since confirmed and extended this classification (35, 51, 55, 62, 105, 115).

The accessory optic tract and the inferior olive

Several pathways distribute visual information to the brainstem and cerebellum (63) and their exact anatomy is not entirely clear. One which has been investigated is the accessory optic tract (AOT). The AOT carries visual information, synapsing in the caudal part of the inferior olive in the medulla, from where the signals are transmitted to the flocculus (22, 23, 30, 60, 68, 75, 88, 89, 90, 114, 128). Animals with lesions in the inferior olive have the same inability to suppress vestibular nystagmus by fixation (74) as animals with lesions in the flocculus (134). Further, lesions of the inferior olive cause reduction of the optokinetic slow phase velocity, indicating that the inferior olive might be important for optokinetic responses (22).

Nucleus prepositus hypoglossi

The nucleus prepositus hypoglossi (NPH) is located in the medulla oblongata, anterior to the hypoglossal nucleus, caudal to the abducens nucleus and medial to the vestibular nuclei. According to Baker & Berthoz (5) the NPH is important for the generation of saccades and visually or vestibularly evoked slow eye movements (5, 6, 7, 58).

Cerebellum

The role of the cerebellum in oculomotor behaviour is

still a matter of some controversy. Nevertheless, there seem to be at least three different regions in the cerebellum taking part in eye motor function: the vestibulo-cerebellum (flocculus, uvula and nodulus), the vermis and the cerebellar nuclei (100). Besides vestibular information, the cerebellum receives visual information via the accessory optic system (89) and other pathways as yet undefined (90).

The present concept of cerebellar function with respect to eye movements is that the cerebellum controls the velocity adaptation of smooth pursuit (83, 134), vestibular slow phase (47, 134) and saccadic amplitude (3, 106). A more detailed description follows:

From observations of oculomotor function in animals with floccular lesions (121, 122, 134) and from single unit recordings (82, 83, 84) it is known that the *flocculus* is able to modify *vestibular responses*. Paradoxically, some investigators find that flocculectomy causes an enhanced slow phase velocity of the vestibulo-ocular responses in darkness (134) while others find the contrary (47). However, a flocculectomy invariably reduces the ability to suppress vestibular nystagmus induced by caloric stimulation (121, 122) or during rotation in light (134).

Experimental studies, in alert monkeys, of single unit activity involving floccular Purkinje cells have been made in recent years. The discharge of these cells during *smooth pursuit* is proportionate to eye velocity (81, 83, 92, 93, 96). Furthermore, floccular lesions impair the velocity of smooth pursuit (134).

Single unit activity related to *saccades* has also been identified in the flocculus (95, 103). According to Burde and coworkers (33) a total cerebellectomy does not alter the velocity of voluntary saccades. The function of the flocculus with reference to saccades is, however, not fully clarified.

In contrast to the wealth of data on the function of the flocculus, little is known about the *uvula* and *nodulus* (52, 100). Both are known to receive visual (113) and vestibular (113) information, and a lesion of either will cause impairment of optokinetic nystagmus (72).

Single unit recordings in the *vermis* have revealed that visual (32, 38, 85) and vestibular information (101) reaches this part of the cerebellum. Further, vermal lesions cause dysmetric saccades (3, 106).

The cerebellar *nuclei* act as relay stations for efferent stimuli from the cerebellum (37) and also for afferent fibers carrying vestibular information (31).

CLINICAL STUDIES OF OCULOMOTOR MECHANISMS

Brainstem disorders

Various oculomotor abnormalities associated with brainstem disease have earlier been investigated (2, 19, 20, 71, 97), but quantitative analyses of eye movements have been performed only during the last two decades (10, 11, 12, 13, 15, 16, 17, 26, 45, 46, 118, 133, 135). According to these investigations brainstem dysfunction may cause reduced smooth pursuit velocity, reduced saccadic velocity, reduced or enhanced slow phase velocity of vestibular nystagmus and reduced slow phase velocity of optokinetic nystagmus (Table I). However, the oculomotor findings described by these authors do show some disparities which may depend on the site or size of the lesion within the brainstem.

Reports concerning the impact of localized lesions within the brainstem on oculomotor function are few. Quantitative analyses have been made of eye movements in patients with internuclear ophthalmoplegia (16, 17, 26) and with lateral medullary infarctions (15). Bird & Leech (26) have shown that internuclear ophthalmoplegia reduced the velocity of the adducting saccade on the side of the lesion, a finding confirmed by Baloh and coworkers (16). In patients with lateral medullary infarctions the peak velocity of voluntary saccades was normal in both directions while smooth pursuit, optokinetic nystagmus, and the ability to suppress vestibular nystagmus, were asymmetrically impaired (15).

Table I. Previously performed quantitative analysis of eye movements in patients with brainstem disorders.

EYE MOVEMENTS	Baloh et al (1975 b) Olivoponto cerebellar degeneration	Bird & Leech (1976) Internuclear ophtalmoplegia	Baloh et al (1977) Brainstem disorders	Baloh et al (1978) Internuclear ophtalmoplegia	Corvera & Romero (1978) Brainstem disorders	Corvera et al (1980) Vertebro basilar insufficiency	Baloh et al (1981) Lateral medullary infarctions
Smooth pursuit velocity	-		Reduced	Normal	-	Reduced	Reduced
Saccade velocity	Reduced	Reduced	Reduced	Reduced	-	-	Normal
Saccade accuracy	-	-	-	-	-	Normal	-
Vestibular nystagmus							
Slow phase velocity	-	-	-	Normal	Reduced	Reduced or Enhanced	Enhanced
Quick phase velocity	-	-			-		
Optokinetic nystagmus							
Slow phase velocity		-	Reduced	Normal	-	Normal	Reduced
Quick phase velocity		-	-	-		-	
Optovestibular nystagmus							
Slow phase velocity	-	-		-	Normal	Normal	Enhanced
Quick phase velocity	-	-			-	-	-

Cerebellar disorders

Various oculomotor abnormalities have been attributed to cerebellar disease and cerebellar dysfunction generally causes inaccuracy of voluntary saccades, reduced velocity of smooth pursuit, reduced slow phase velocity of optokinetic nystagmus, enhanced slow phase velocity of vestibular nystagmus and occasionally causes reduced velocity of voluntary saccades (Table II)(11, 12, 18, 50, 112, 116, 125, 133, 135). The occurrence of disturbances in different types of eye movements has not been without disparities, which may depend on the type of disorder examined.

The fast phases of nystagmus have not received much attention. In one investigation of spinocerebellar degeneration Zee and coworkers (133) found reduced velocities in voluntary saccades and in fast phases of vestibular nystagmus.

According to most authors the velocity of smooth pursuit and slow phase of optokinetic nystagmus is reduced in patients with cerebellar disease. In patients with hereditary cerebellar ataxia, however, according to Zee and coworkers (135), the velocity of the slow phase in optokinetic nystagmus, although reduced, is less affected than smooth pursuit velocity. This finding indicates that the two types of eye movements, slow phases of optokinetic nystagmus and smooth pursuit, are not equally dependent on cerebellar function, as has also been suggested by Honrubia (69).

Most studies, including those cited above, deal with complex cerebellar disorders such as spinocerebellar degeneration (125, 133), hereditary cerebellar ataxia (135), cerebellar atrophy (11, 12) or Arnold-Chiari malformation (18, 116) - all diseases known to involve brainstem regions, at least in advanced stages. Furthermore, as the cerebellum gets its vascular supply via

Table II. Previously performed qualitative and quantitative analysis of eye movements in patients with cerebellar disorders.

EYE MOVEMENTS	Wadia & Swami (1971) Spinocerebellar degeneration	Ellenberger et al (1972) Cerebellar disease	Baloh et al (1975 a) Cerebellar atrophy	Selhorst et al (1976) Cerebellar tumours	Zee et al (1976 a) Spino-cerebellar degeneration	Zee et al (1976 b) Cerebellar ataxia	Baloh et al (1979) Cerebellar atrophy	Baloh et al (1981) Cerebellar atrophy Arnold Chiari malformation	Spooner & Baloh (1981) Arnold Chiari malformation
Smooth pursuit velocity	Reduced	Normal	Reduced	-	Reduced	Reduced	-	Reduced	Reduced
Saccade velocity	Reduced	Normal	Reduced	Normal	Reduced	Normal	-	Normal	Normal
Saccade accuracy	-	Reduced	Reduced	Reduced	-	Reduced	-	-	Normal
Vestibular nystagmus									
Slow phase velocity	-	-	Enhanced	-	Normal	Enhanced	Normal or Enhanced	Enhanced	Enhanced
Quick phase velocity	-	-	-	-	Reduced	-	-	-	-
Optokinetic nystagmus									
Slow phase velocity	Reduced	-	Reduced	-	Normal	Reduced	Reduced	Reduced	Reduced
Quick phase velocity	Reduced	Normal	-	-	Reduced	-	-	-	-
Optovestibular									
Slow phase velocity	-	-	-	-	-	-	Reduced	Reduced	Normal
Quick phase velocity	-	-	-	-	-	-	-	-	-

the circumflex branches from the vertebro-basilar arteries, a proximally located arterial occlusion may also affect the brainstem, which should be considered when vascular pathophysiology is involved. It also follows that lesions restricted to the cerebellum and without concomitant brainstem involvement are rare.

Aims of the present study

Quantitative analyses of eye movements in patients with brainstem and cerebellar disease have been made before, but detailed information about the site of the lesion has seldom been available, nor have systematic studies of all types of horizontal conjugate eye movements been made in one and the same investigation.

The aims of the present study were therefore:

1. to study the abnormalities of horizontal conjugate eye movements associated with disorders in the brainstem (I).

2. to correlate these abnormalities with the anatomical sites of the lesions within the upper, middle or lower brainstem (II).

3. to study oculomotor abnormalities of patients with cerebellar disease with or without concomitant brainstem involvement (III).

4. to evaluate oculomotor abnormalities in patients diagnosed as suffering from vestibular neuronitis, and to try to determine the site of lesion by means of eye movement analysis and neurological examination (IV).

Material

PATIENTS WITH BRAINSTEM DISORDERS (I, II)

I. Ten patients, 4 males and 6 females whose ages ranged from 17 to 73 with a mean of 61 years, with brainstem disorders were examined with electro--oculography. Seven of the patients suffered from infarctions, 2 from progressive supranuclear palsy (PSP) and one from a tumour (Table III).

II. Thirty patients, 20 males and 10 females whose ages ranged from 17 to 81 with a mean of 63 years, with defined lesions within the brainstem were examined with electro-oculography. Some of the patients were included in the previous study (I). The patients were divided into three different groups depending on the site of the lesion. Five patients suffered from progressive supranuclear palsy (PSP). Of the 15 patients with lesions in the pons, 11 were cases of infarction, 3 of tumours, and 1 of encephalitis. Of the 10 patients with lesions in the medulla oblongata, 8 suffered from lateral and 2 from medial infarctions (Table III).

PATIENTS WITH CEREBELLAR DISORDERS (III)

Twelve patients, 5 males and 7 females whose ages ranged from 27 to 69 with a mean of 45 years, were examined with electro-oculography (Table III). Neurological examination revealed 6 with evidence of concomitant brainstem involvement. Those with signs or symptoms restricted to the cerebellum

Table III. Site of lesion, diagnosis, number of patients and range of age of the patients in studies I-III.

Study	Site of lesion	Diagnosis			No of pat.	Age (range)
I	Brainstem	PSP			2	17-73
		infarction			7	
		tumour			1	
II	Brainstem	PSP			5	17-81
		pontine	infarction		11	
			tumour		3	
			encephalitis		1	
		medullary	infarction	lateral	8	
				medial	2	
III	Cerebellum	atrophy			2	39-53
		infarction			1	
		hematoma			1	
		metastasis			1	
		multiple sclerosis			1	
	Cerebellum-brainstem	tumour			2	27-69
		metastasis			1	
		infarction			1	
		degenerative disease			1	
		encephalitis			1	

consisted of 2 with cerebellar cortical atrophy, 1 infarction, 1 hematoma, 1 metastasis, and 1 multiple sclerosis. Of the 6 patients with concomitant brainstem involvement 2 had tumours, 1 a metastasis, 1 an infarction, 1 degenerative disease and 1 encephalitis with both cerebellar and brainstem manifestations.

PATIENTS WITH VESTIBULAR NEURONITIS (IV)

Thirty patients, 14 males and 16 females whose ages ranged from 23 to 69 with a mean of 51.9 years, diagnosed as suffering from vestibular neuronitis were analyzed with electro-oculography. All patients were examined by a neurologist and in 9 cases the cerebrospinal fluid was analyzed.

In the studies I-IV 20 healthy subjects, 10 males and 10 females whose ages ranged from 23 to 72 with a mean of 48 years, were used as controls. The control subjects had no history of previous vestibular or neurological disease. This material has been published earlier (67, 109).

Methods

TEST PROCEDURE

Voluntary saccades were elicited using light-emitting diode targets positioned 5, 10, 20, 30, 40, and 60° apart on a horizontal bar placed 120 cm in front of the patient.

Smooth pursuit was elicited using a target consisting of a moving light spot 3 cm in diameter projected on a horizontal screen placed 160 cm in front of the patient. The movement of the target covered a visual angle of 60°, with target velocities of 10, 20, 30, 40, 50, and $60^{\circ}s^{-1}$.

Vestibular nystagmus was induced by rotating the patient in a revolving chair with an acceleration and deceleration of $120^{\circ}s^{-2}$. The velocity of the chair was $120^{\circ}s^{-1}$ when fully accelerated and the test was performed in darkness.

Optokinetic nystagmus was induced with the patient seated inside a cloth drum of 180 cm diameter, with alternating black and white vertical stripes 10 cm in width. The drum was accelerated for 10 seconds to a maximum velocity of $90^{\circ}s^{-1}$.

Optovestibular nystagmus was induced by rotating the patient as in the rotation test but in light with open eyes and inside the stationary optokinetic drum.

The caloric test was performed in darkness with open eyes and with water temperatures of $30^{\circ}C$ and $44^{\circ}C$.

During the whole test procedure the patient sat comfortably in a chair with the head supported and was observed through an infrared TV-camera. The tests were operated by a specially trained assistant and lasted for about 90 minutes. Verbal and visual contact with the patient was maintained throughout the whole procedure, in order to control the level of alertness.

RECORDING OF EYE MOVEMENTS (I-IV)

The eye movements were recorded with a d.c. electro-oculographic technique using an ink-jet writer with six channels (Mingograph M 81, Siemens Elema, Stockholm, Sweden) with a low-pass filter of 15 Hz. The speed of the paper was 100 mm s^{-1} during recording of saccades and nystagmus and 25 mm s^{-1} during recording of smooth pursuit, the former having a scale of 1 mm to 10 ms along the time axis and the latter 1 mm to 40 ms. The recording permitted the resolution of eye position to an accuracy of 1^{o}, corresponding to 1 mm on the recording sheet. Calibrations were made twice during the test. We used commercially available Ag/AgCl electrodes mounted in a plastic cup (Medicotest^{R}). The space between the electrode and the skin was filled with electrolytic paste. Before application of the electrodes, the outer keratin layer of the skin was removed with a drill. Electrodes for recording horizontal eye movements were placed near the outer canthi in order to record both eyes simultaneously. The electrodes for recording vertical eye movements were placed above each eye to record each eye separately.

ANALYSIS OF THE RECORDINGS (I-IV)

The peak velocity of voluntary saccades and fast phases of nystagmus was measured by estimating the

tangent of the recorded eye movement (67). In any one patient at least 5 consecutive saccades at each amplitude and direction were measured. The peak velocity of the fast phases of nystagmus was measured for 10 s of the nystagmus reaction. Since the velocity of rapid eye movements is related to the amplitude, the peak velocities were arranged in six different groups with mean amplitudes of 5, 10, 20, 30, 40, and 60° (67). The accuracy of the saccade was measured at amplitudes of 20 and 60° and was expressed as the amplitude of the initial saccade and compared with the corresponding mean amplitudes in 20 normal subjects (66).

Maximum velocity of the slow phase of nystagmus was measured at the response culmination. Smooth pursuit velocity was measured at its highest velocity and a period of 250 ms without superimposed saccades was required. The period of 500 ms at the start of the smooth pursuit was not considered because of velocity adaptation (109). The maximum velocity gain of smooth pursuit was calculated as the ratio of maximum eye velocity to target velocity. The total number of superimposed saccades during tracking to the right and left at target velocities of 10, 20, 30, 40, 50, and 60° were estimated and compared with corresponding data from 20 normal subjects (109).

STATISTICS

A. Statistics for individual patients

The mean of the eye velocities in the various types of eye movements in 20 healthy subjects ± 2 standard deviations was used as the normal range. In the recordings of smooth pursuit, voluntary saccades and fast phases of nystagmus where data were collected from several measuring points, at least 2 of 6 values

were required to be outside the above mentioned normal range to be considered pathological. The probability of one of 6 values being an outlier of the normal range is 26% and for 2 of 6 values less than 5% (79). In eye movements where data could be collected only from one measuring point as in the slow phases of nystagmus, a value found outside the normal mean ± 2 standard deviations was considered pathological. Thus the probability for each type of eye movement of a normal subject being classified as pathological by chance alone was 5% or less. The same kind of evaluation has been used by other investigators (14, 27).

B. Statistics for groups of patients

Student's t-test for unpaired data was used when eye velocity statistics for normal subjects and groups of patients were calculated (II). As a further test for statistically significant differences, the distribution of reduced and enhanced velocities in each type of eye movement was calculated using chi-square (χ^2) tests. Results at the 5% probability level were regarded as statistically significant.

Results

EYE MOVEMENTS IN BRAINSTEM LESIONS (I)

In 10 patients with disorders in the brainstem reduced maximum velocities of smooth pursuit were found in all cases and reduced peak velocities of voluntary saccades in all except one. In nystagmus, reduced velocities were most frequent in slow phases of optovestibular nystagmus (7/9), slow phases of optokinetic nystagmus (6/10) and fast phases of vestibular nystagmus (6/10). Conversely, the most often preserved eye movement was the fast phase of optokinetic nystagmus, being reduced in only one patient.

A marked dissociation in the vulnerability of the optokinetic nystagmus between the slow phase on one hand and the fast phase on the other was found. Dissociations were also noted in other types of eye movements (Fig. 3).

EYE VELOCITY PROGRAMMING IN BRAINSTEM DISORDERS (II)

The 5 patients with *progressive supranuclear palsy* showed reduced maximum velocity of smooth pursuit and an increased number of superimposed saccades during tracking. All these patients also had reduced saccadic velocities (Fig. 3) and inaccuracy of voluntary saccades. In nystagmus, reduced velocities were most common in the slow phases of optokinetic nystagmus (5/5) and optovestibular nystagmus (4/4) and the fast phases of optovestibular nystagmus (3/4)(Fig. 3).

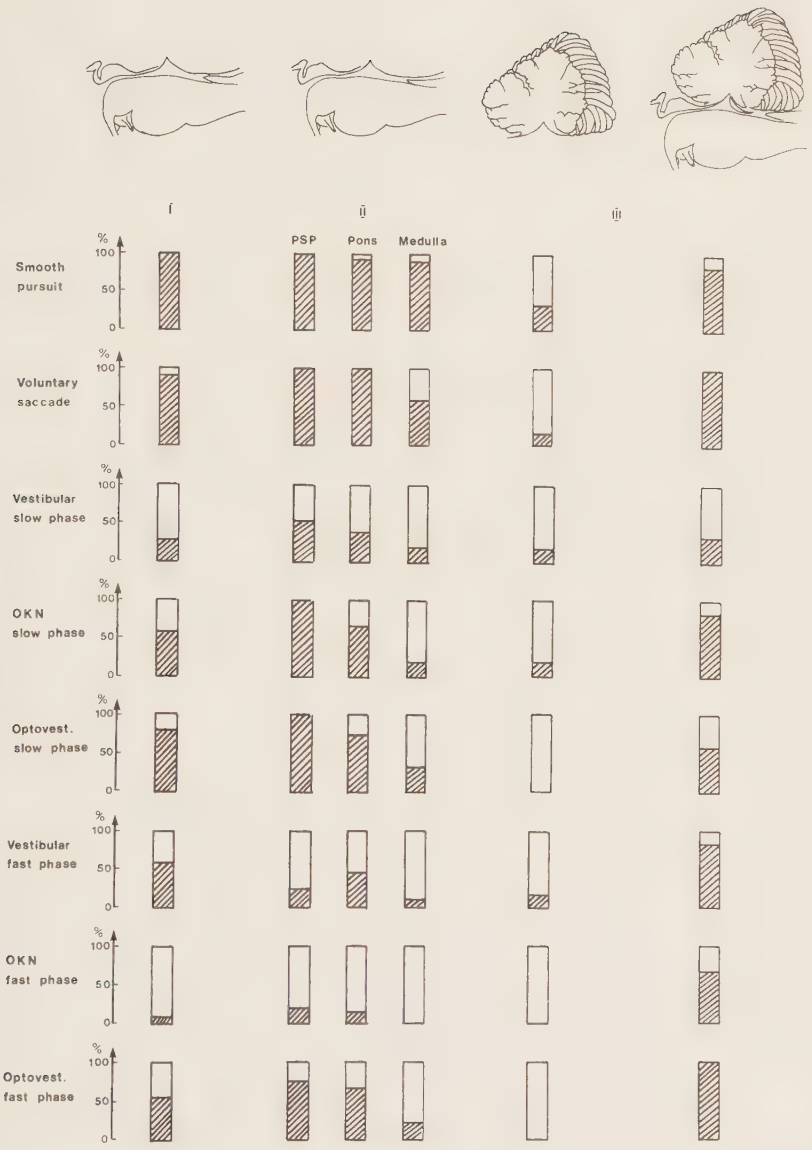


Fig. 3. Percentage of cases with significantly reduced eye movement velocities in study I (brainstem), in study II (upper, middle and lower brainstem) and in study III (cerebellum and combined cerebello-brainstem). Dashed areas indicate cases with reduced velocities. PSP = progressive supranuclear palsy.

Fig. 4. Percentage of cases with significantly enhanced eye movement velocities in study I, II and III. Black areas indicate cases with enhanced velocities. PSP = progressive supranuclear palsy.

In the *pontine group* 14 of the 15 patients showed reduced maximum velocity of smooth pursuit. The number of superimposed saccades during tracking was above normal in 9 of 15 patients. All patients had reduced saccadic velocity. Inaccuracy of voluntary saccades was found in 10 of 15 patients. In nystagmus, reduced velocities were most common in the slow phases of optovestibular nystagmus (9/12), the fast phases of optovestibular nystagmus (8/12), and the slow phases of optokinetic nystagmus (10/15)(Fig. 3).

Of the 10 patients with *medullary disorders*, all but one showed reduced maximum velocity of smooth pursuit. The number of superimposed saccades during tracking was above normal in 8 of 10 patients. Six of 10 patients had reduced saccadic velocity and one had an enhanced saccadic velocity. Inaccuracy of voluntary saccades was found in 3 of 10 patients. In nystagmus, reduced velocities were most common in the slow phases of optovestibular nystagmus (3/9). Enhanced velocities were found in the fast phases of optokinetic nystagmus (3/10), the slow phases of optovestibular (1/9) and optokinetic (1/10) nystagmus, and in the fast phases of vestibular nystagmus (1/10)(Fig. 3, 4).

To test whether the frequencies of pathological velocities in various eye movements in patients with PSP, pontine and medullary disorders differed significantly chi-square tests were carried out. These revealed statistically significant differences in frequency of reduced velocities of voluntary saccades and slow phases of optokinetic and optovestibular nystagmus when PSP, pontine disorders and medullary disorders were compared (Table IV).

Further, enhanced responses of the fast phase of optokinetic nystagmus were more frequently found in medullary disorders than in PSP and pontine disorders $\left[\chi^2\ (2) = 6.67,\ p<0.05\right]$. These results were in good agreement with the results of Student's t-test (II).

Table IV. Results in χ^2 tests of frequency differences in reduced velocities in various eye movements in PSP, pontine and medullary disorders.

TYPES OF EYE MOVEMENTS	χ^2	degrees of freedom	p
Smooth pursuit	0.54	2	n.s.
Voluntary saccade	9.23	2	< 0.01
Slow phase of vestibular nystagmus	2.44	2	n.s.
Slow phase of optokinetic nystagmus	9.91	2	< 0.01
Slow phase of optovestibular nystagmus	6.55	2	< 0.05
Fast phase of vestibular nystagmus	3.85	2	n.s.
Fast phase of optokinetic nystagmus	1.85	2	n.s.
Fast phase of optovestibular nystagmus	5.08	2	n.s.

EYE MOVEMENTS IN CEREBELLAR AND COMBINED CEREBELLO--BRAINSTEM DISEASES (III)

Two of the 6 patients with *cerebellar disease* showed reduced maximum velocity of smooth pursuit and the number of superimposed saccades was above normal in 2 patients. One of them had normal smooth pursuit velocity while the other had a significantly reduced velocity. One of 6 patients had reduced saccadic velocity while an enhanced velocity was found in one patient. Inaccuracy of voluntary saccades, primarily hypometria, was found in 3 of 6 patients. In nystagmus, reduced velocities were most common in the fast (1/6) and slow (1/6) phases of vestibular nystagmus and in the slow phase of optokinetic nystagmus (1/6). Enhanced velocities were most common in the vestibular slow phase (5/6) and the optokinetic fast phase (5/6) (Fig. 3, 4).

Five of 6 patients with *cerebello-brainstem disease* showed a reduced maximum velocity of smooth pursuit and the number of superimposed saccades was above normal in 5 of 6 patients. All patients had reduced

saccadic velocity and inaccuracy of the voluntary saccades. In nystagmus, reduced velocities were most common in the fast phases of optovestibular (5/5) and vestibular (5/6) nystagmus and the slow phases of optokinetic nystagmus (5/6). Enhanced velocities were found in the fast phases of vestibular nystagmus (1/6) (Fig. 3, 4).

The difference in how frequently reduced and enhanced velocities in various types of eye movements in cerebellar and combined cerebello-brainstem disease appeared (Fig. 3, 4) was calculated using chi-square tests. The distribution of reduced velocities was significantly different for all types of eye movements except smooth pursuit and slow phases of vestibular nystagmus (Table V) and was most common in combined cerebello-brainstem disease.

Consistently, enhanced responses occurred more often in cerebellar disease than in combined cerebello-

Table V. Results in χ^2 tests of frequency differences in reduced velocities in various eye movements in cerebellar and combined cerebello-brainstem disease.

TYPES OF EYE MOVEMENTS	χ^2	degrees of freedom	p
Smooth pursuit	3.09	1	n.s.
Voluntary saccade	8.57	1	< 0.01
Slow phase of vestibular nystagmus	0.44	1	n.s.
Slow phase of optokinetic nystagmus	6.20	1	< 0.05
Slow phase of optovestibular nystagmus	4.95	1	< 0.05
Fast phase of vestibular nystagmus	5.33	1	< 0.05
Fast phase of optokinetic nystagmus	6.00	1	< 0.05
Fast phase of optovestibular nystagmus	11.00	1	< 0.01

-brainstem disease. Statistically significant differences between cerebellar disease and combined cerebello-brainstem disease in enhanced responses were found in the slow phases of vestibular $\left(\chi^2\ (1) = 8.57,\ p<0.01\right)$ nystagmus and in the fast phases of optokinetic $\left(\chi^2\ (1) = 8.57,\ p<0.01\right)$ and optovestibular $\left(\chi^2\ (1) = 4.95,\ p<0.05\right)$ nystagmus.

COMPARISON OF EYE VELOCITY PATTERNS BETWEEN DIFFERENT GROUPS OF PATIENTS (II, III)

In order to estimate whether the observed differences between pontine and cerebellar disorders (Fig. 3, 4) were statistically significant chi-square tests were carried out. Results for reduced responses, most commonly found in pontine disorders, are shown in Table VI and for enhanced responses, most commonly found in cerebellar disorders, in Table VII. Statistically significant differences in pathological

Table VI. Results in χ^2 tests of frequency differences in reduced velocities in various eye movements in pontine and cerebellar disorders.

TYPES OF EYE MOVEMENTS	χ^2	degrees of freedom	p
Smooth pursuit	8.51	1	< 0.01
Voluntary saccade	16.41	1	< 0.01
Slow phase of vestibular nystagmus	1.05	1	n.s.
Slow phase of optokinetic nystagmus	4.30	1	< 0.05
Slow phase of optovestibular nystagmus	9.00	1	< 0.01
Fast phase of vestibular nystagmus	1.64	1	n.s.
Fast phase of optokinetic nystagmus	0.89	1	n.s.
Fast phase of optovestibular nystagmus	7.20	1	< 0.01

Table VII. Results in χ^2 tests of frequency differences in enhanced velocities in various eye movements in pontine and cerebellar disorders.

TYPES OF EYE MOVEMENTS	χ^2	degrees of freedom	p
Smooth pursuit	-	1	n.s.
Voluntary saccade	2.63	1	n.s.
Slow phase of vestibular nystagmus	16.41	1	<0.01
Slow phase of optokinetic nystagmus	5.53	1	<0.05
Slow phase of optovestibular nystagmus	-	1	n.s.
Fast phase of vestibular nystagmus	8.75	1	<0.01
Fast phase of optokinetic nystagmus	16.41	1	<0.01
Fast phase of optovestibular nystagmus	8.74	1	<0.01

velocities between pontine and cerebellar disorders were found in all types of eye movements.

However, the difference was not apparent if a cerebellar disorder encroached upon brainstem structures. Thus, between pontine and combined cerebello-brainstem disorders statistically significant differences were only found in the fast phases of optokinetic nystagmus $\left(\chi^2\ (1) = 5.97,\ p<0.05\right)$.

The medullary patients exhibited to some extent oculomotor abnormalities resembling those found in patients with cerebellar disease (Fig. 3, 4). Chi-square tests, however, revealed statistically significant differences for reduced responses in smooth pursuit $\left(\chi^2\ (1) = 5.60,\ p<0.05\right)$ and for enhanced responses in the slow phases of vestibular $\left(\chi^2\ (1) = 12.1,\ p<0.01\right)$ nystagmus and fast phases of optokinetic $\left(\chi^2\ (1) = 4.27,\ p<0.05\right)$ and optovestibular $\left(\chi^2\ (1) = 6.87,\ p<0.01\right)$ nystagmus.

VESTIBULAR NEURONITIS - A CLINICAL AND ELECTRO--OCULOGRAPHIC ANALYSIS (IV)

Thirty patients with vertigo as the only initial symptom were on routine examination considered to suffer from vestibular neuronitis. Neurological examination revealed signs of a disorder within the central nervous system in 4 cases. Furthermore, in 2 patients examination of the cerebrospinal fluid showed changes compatible with multiple sclerosis or infectious CNS disorders. In altogether 12 patients an electro-oculographic analysis showed oculomotor abnormalities compatible with those found in patients with central nervous system disorders. These findings consisted of reduced maximum velocity gain of smooth pursuit (maximum eye velocity/target velocity) in 10 patients, reduced saccadic velocity in 9 patients and reduced optokinetic slow phase velocity in 4 patients. Altogether 13 out of 30 patients exhibited some evidence of possible involvement of the central nervous system. Predisposing risk factors for cerebro-vascular accidents were observed in 8 of these 13 patients.

Discussion

An analysis of eye movements in patients with lesions in the upper (PSP) or middle (pontine disorders) brainstem revealed that these patients had reduced velocity of smooth pursuit and voluntary saccades and frequently also of slow and fast phases of nystagmus (I, II).

Patients with lesions in the lower brainstem (medullary disorders) had reduced smooth pursuit velocity. Their saccadic velocity was usually reduced, although there were cases of normal or even enhanced velocities. In the various types of nystagmus normal velocities predominated (II) but occasionally reduced or enhanced velocities were found.

Patients with cerebellar disease had normal or reduced smooth pursuit velocity and normal saccadic velocity in the majority of cases. Velocities in different types of nystagmus were frequently normal or even enhanced (III).

Patients with combined cerebello-brainstem disease had reduced velocities of smooth pursuit and voluntary saccades and frequently also of slow and fast phases in different types of nystagmus (III).

Patients diagnosed as suffering from vestibular neuronitis revealed signs of intrinsic central nervous system disease when electro-oculographic and neurological examinations were performed (IV). The patients with vestibular neuronitis seem therefore to represent a disease entity with different pathophysiology.

COMMENTS ON METHODS

Electro-oculography, the method most commonly found in clinical practice, was introduced by Schott in 1922 (111) and further developed by Meyers (91) and Jacobson (76). It is based upon potential differences between skin electrodes generated by the corneo--retinal potential and has the advantage of being able to record eye movements in light or in darkness with eyes open or closed. The technique, however, has some disadvantages. The recorded potential is disturbed by noise from electric power sources and by muscle and brain activity. Alternative methods are based on corneal reflection, limbus, pupil and eyelid tracking, and techniques employing contact lenses (131). For various reasons, such as time-consuming adjustment of the equipment, discomfort for the patient or, with contact lenses, the risk for slipping or corneal damage, these methods are less common in routine clinical work (37, 130, 131).

Photoelectric recordings reveal much higher peak velocities of voluntary saccades than electro--oculographic recordings (27). Therefore results in different studies are only comparable if the same recording technique is used.

COMMENTS ON SELECTION OF PATIENTS

Topographical diagnosis was ascertained by careful analysis of the history combined with repeated neurologic examinations paying special attention to any oculomotor or other cranial nerve dysfunction as well as involvement of the long motor and sensory tracts. Furthermore, the patients were scrutinized for any evidence of cerebellar dysfunction, such as truncal or gait ataxia, i.e. abnormalities of gait or stance, dysmetria of voluntary movements and

dysdiadochokinesis. The work-up included neuro--ophthalmological examination and in most patients neuro-radiological examinations, i.e. vertebral angiography, pneumo-encephalography or computerized axial tomography (CT).

The classification of patients in the present study was based mainly on neurological examination since computerized axial tomography of the posterior fossa frequently fails to reveal the lesion, particularly when this is localized within the brainstem (34, 43). The clinician who attempts to delineate lesions in the posterior fossa frequently has difficulties, particularly with regard to the extent of combined cerebello-brainstem disorders. Lesions in the brainstem may impinge on pathways carrying information to or from the cerebellum, thus mimicking a cerebellar disorder. Correspondingly a cerebellar mass lesion may compress or even encroach upon brainstem structures. Therefore some topographical overlapping between the cerebellar, cerebello-brainstem, pontine and medullary groups cannot be completely ruled out.

SMOOTH PURSUIT AND OPTOKINETIC SLOW PHASES IN POSTERIOR FOSSA DISORDERS

Reduced maximum velocities of smooth pursuit were almost uniformly found in patients with lesions in the upper, middle and lower brainstem (II). This is in agreement with previous investigations of patients with brainstem disorders (10) and a recent study of patients with lateral medullary infarctions (15).

The reason for reduced smooth pursuit velocities in patients with disorders of the upper brainstem (II) is not known but might be due to malfunctioning of visual feedback mechanisms (107), while patients with pontine disorders (II) may lack normal activity in the

velocity encoding mechanisms in pons (87). Reduced smooth pursuit velocity in medullary disorders in humans (II) may be ascribed to dysfunction of the inferior olive or nucleus prepositus hypoglossi (132). Experimental lesions of the inferior olive have an adverse effect on visually evoked slow eye movements, similar to that found in floccular lesions (22). More recently also the nucleus prepositus hypoglossi has been assigned a role in the control of slow eye movements (7).

Various authors have postulated that cerebellar dysfunction causes reduced smooth pursuit velocity (12, 110, 135). Experimentally it has been shown that neurons in flocculus discharge during smooth pursuit eye movements (81, 83, 92). Consequently the finding of normal smooth pursuit velocity in the majority of the patients with cerebellar disease in the present study (III) might indicate that the flocculus in these patients was not involved. Alternatively, the cerebellar dysfunction in the patients in the present investigation might have been compensated for by mechanisms elsewhere. A cerebellar lesion has a marked tendency to be compensated for in the course of time. As a result cerebellar oculomotor defects are variable (123, 129). It must, however, be pointed out that previous studies in humans mainly deal with patients with degenerative diseases where compensation is not plausible nor can concomitant brainstem involvement be excluded (Table II). This might be an explanation as to why reduced smooth pursuit velocities have so frequently been found.

Reduced slow phase velocities of optokinetic nystagmus were more common in patients with pontine than in patients with medullary disorders, whereas smooth pursuit velocities were reduced in both groups (Fig. 3). This supports the idea of different mechanisms being behind these two types of visually evoked slow eye

movements (28, 69, 70, 94). The present findings of normal optokinetic slow phases in patients with medullary disorders (II) may indicate that optokinetic responses are not dependent on an intact medullary function, whereas smooth pursuit is. Thus, dysfunction of the inferior olive or nucleus prepositus hypoglossi does not seem to produce defective optokinetic responses in humans.

VOLUNTARY SACCADES AND FAST PHASES OF NYSTAGMUS IN POSTERIOR FOSSA DISORDERS

As velocity encoding of rapid eye movements apparently takes place in the paramedian pontine reticular formation (42, 78), pontine disorders should cause defects of rapid eye movements (10, 13). Reduced velocity of voluntary saccades was consistently found if the disorder was located in the pontine region (I, II). The accepted view that all types of rapid eye movements are disturbed to the same degree because of identical velocity encoding mechanisms (62, 78) proved impossible to confirm. Instead a marked dissociation was found. The velocity of the fast phases of nystagmus was unimpaired in some cases of pontine disorders while the velocity of saccades was reduced in all cases. This indicates somewhat different mechanisms behind the velocity encoding of voluntary saccades and fast phases of nystagmus at the pontine level, as has been pointed out in a previous study (67).

In medullary lesions, a reduced velocity of voluntary saccades was found in some cases, although not as frequently as in cases of pontine disorder (II). This indicates that lesions in the medulla oblongata may in some cases disturb the velocity encoding mechanisms of voluntary saccades. The nucleus prepositus hypoglossi in the medulla may contain substrates participating in the velocity control of rapid eye move-

ments, as has been suggested by Baker and coworkers (7) after experimental studies. However, exact conclusions cannot be drawn with reference to humans even though the present investigation gives support for such an idea.

In patients with cerebellar disease (III) saccadic velocity was reduced only occasionally. The present observations support previous results which indicate that a cerebellar lesion does not normally cause reduced saccadic velocity (18, 50, 135). Reduced velocities of voluntary saccades described by others (12, 125) probably depend on extension of the disease outside the cerebellum.

There is no previous report on enhanced velocities of fast phases of nystagmus in cases of cerebellar or medullary disease (II, III). A similar enhancement of the velocity in voluntary saccades has recently been observed in patients with encephalitis (66) and in patients exposed to industrial solvents (98). The conventional view is that neither cerebellum nor medulla oblongata participate in the velocity encoding of rapid eye movements. There is, however, some experimental support for the present findings. Ron & Robinson (108) could by cerebellar stimulation produce hypometric saccades in monkeys with a velocity equivalent to one of unimpaired amplitude and consequently much higher than in a normal saccade. Further support was gained from experiments made by Ritchie (106), who with vermal lesions in the monkey observed that saccades were hypometric and that there was a dissociation between saccadic amplitude and duration, which means that some saccades had an enhanced velocity. Since the velocity is related to the amplitude this would simulate the enhancement in velocity which we found in patients with cerebellar disease (III). Similar findings in cases with medullary lesions (II) may be due to an impact on the pathways passing to or from the cerebellum.

The accuracy of voluntary saccades was most frequently impaired in patients with combined cerebello-brainstem disorders (III), followed by patients with pontine disease (II) and cerebellar disease (III) but only occasionally in patients with medullary lesions (II). Saccades were mainly hypometric, and hypermetria was not common. Hence it appears that structures within the pons and cerebellum participate in the modulation of amplitudes of saccades but their specific function in this aspect is not known (8, 106, 133).

VESTIBULAR NEURONITIS - A DISEASE ENTITY?

As has been shown in the present investigation (IV), vertigo can be a particularly difficult symptom to assess. In patients with occlusion of the vertebro--basilar arteries, vertigo is frequently the first and in 25% of cases an unaccompanied symptom (29, 53). Thus, a vascular etiology of vertigo must always be considered.

The etiology of vestibular neuronitis remains in doubt. The disorder has been linked to infection (39, 48), but also to vascular pathology (80). In the present investigation, predisposing risk factors for cerebrovascular accidents were more common in those patients who showed oculomotor signs of a "central" cause of the vertigo than in patients with a "peripheral" cause. This may imply that in cases of vascular accident the site is located in the brainstem and not in the labyrinth. The degenerative changes found in the labyrinths by Lindsay & Hemenway (80) may have been secondary to vascular changes in the brainstem.

The present study agrees with Hart (61) and Pfaltz & Meran (99) in restricting the use of the term vestibular neuronitis to cases without intercurrent disease predisposing for cerebrovascular accidents

and without "central" signs in the electro-oculographic analysis. In the remaining cases the disease should be named "sudden vertigo" or "vestibular paralysis of sudden onset" (61), until the site of the lesion is localized.

Conclusions

An analysis of eye movements in patients with lesions in the upper (PSP) or middle (pontine disorders) brainstem (II) and in patients with combined cerebello--brainstem disorders (III) revealed that these patients had reduced velocities in smooth pursuit and voluntary saccades and frequently also in slow and fast phases of various types of nystagmus. The eye velocity pattern found in these groups was significantly different from the eye velocity pattern in the medullary and cerebellar groups.

Patients with medullary disorders are distinguished from the previous groups by in some cases normal saccadic velocity and more frequently normal or even enhanced velocities in various types of nystagmus (II).

The oculomotor abnormalities in cerebellar disease (III) showed a superficially similar pattern, although smooth pursuit velocity was more often found to be normal and the velocities in the slow phases of vestibular and fast phases of optokinetic and optovestibular nystagmus were more frequently enhanced than in medullary disorders. These differences were statistically significant.

When electro-oculographic analysis was performed on 30 patients diagnosed as suffering from vestibular neuronitis, 12 revealed signs of an intrinsic CNS disease. In 11 of these cases predisposing risk factors for cerebrovascular accidents and neurological examination supported a "central" cause of the vertigo (IV).

Information achieved by studying oculomotor abnormalities in posterior fossa disorders may add to our understanding of the function of the oculomotor system in humans. In addition, an analysis of eye movements provides information on the localization of a disorder in the posterior fossa.

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EYE MOVEMENTS IN BRAINSTEM LESIONS

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bstract. The eye movements of 10 patients with brain-tem lesions were examined, using an electro-oculo-raphic technique. An analysis was made of the responses n the following tests: smooth pursuit, saccade, rotation, ptokinetic, optovestibular and caloric. Chief interest was irected towards the peak velocity. The results were com-ared with the corresponding velocities in 20 normal sub-cts. In the same patient, one or several types of eye ovements could be normal, while others were pathologi-al. In the whole group, voluntary eye movements mooth pursuits and voluntary saccades) were more vul-erable than reflexive ones (nystagmus). Next to the nooth pursuit test and the voluntary saccade test, the op-vestibular test was the most sensitive in discriminating atients with brainstem lesions from normal subjects.

umerous neurons in and between the vesti-ular nuclei, the paramedian pontine reticular ormation (PPRF) and the eye motor nuclei are volved in the control of eye movements Raphan & Cohen, 1978).

The PPRF is considered to be the major tar-et for most of these neurons (Bender & hanzer, 1964;, Cohen & Feldman, 1968; Co-en et al., 1968). In the PPRF, *phasic* units, ctive during fast eye movements, are located n the rostral part, and *tonic* units, active du-ng slow eye movements, are located more audally or around the abducens nucleus Luschei & Fuchs, 1972; Keller, 1974; Henn Cohen, 1975). The same phasic units dis-harge before any fast eye movement, either isually or vestibularly, evoked (Keller, 1974). uring fixation all saccades are inhibited by *ausing* units scattered throughout the PPRF Keller, 1974).

The aim of this study was to find out how arious types of eye movement were disturbed patients with brainstem lesions. It also was our intention to map out how various distur bances in the velocities of eye movement were combined.

MATERIAL AND METHODS

The material consisted of 10 consecutive pa tients with brainstem lesions who were thor oughly examined by a neurologist. The diag nosis was based on case history and neurologi cal findings. Whenever possible the lesion wa topographically defined. The work-up includ ed computerized tomography, EEG, neuro ophthalmological and neuro-otological exa minations. Seven patients had brainstem in farctions at various sites, 2 had progressiv supranuclear palsy and one had a tumour i the fourth ventricle.

Twenty healthy subjects whose ages range from 23 to 72 (mean age 48) years were use as controls.

Smooth pursuit eye movements were in duced by projecting a light spot of 30 mm dia meter, covering an angle of 1.05 rad, on screen. The spot moved at constant velocitie of 0.17, 0.35, 0.52, 0.70, 0.87 and 1.05 rad s in front of the patient and a new spot was sub stituted when the other one disappeared. A least five recordings were made at each velo city and direction (Schalén, 1980).

Voluntary saccades were induced by askin the patient to look at light diodes placed hor zontally in front of the subject at angles o 0.08, 0.17, 0.35, and 0.52 rad on both sides o the midline (Henriksson et al., 1980), th patient being told to look alternatingly as fas

Table I. *A summary of the velocity patterns of different eye movements in all the patients*

Age, type and site of lesion are described. Fast = fast phase velocity. Slow = slow phase velocity. DP = directio preponderance. CP = canal paresis. N = normal. ↓ = decreased

t.	Age	Type of lesion	Side	Level	Pur-suit velo-city	Sac-cade velo-city	Rota-tion fast	Rota-tion slow	OKN fast	OKN slow	Opto-vest fast	Opto-vest slow	Caloric slow
A.	65	Vascular	Right	Lateromed.	↓	↓	↓	N	N	N	N	N	DP right
A.	17	Tumour	Bilateral	Pontine	↓	↓	↓	↓	↓	↓	–	–	CP left
H.	71	PSP	Bilateral	Supranuclear	↓	↓	↓	N	N	N	↓	↓	CP left
J.	66	Vascular	Bilateral	Medullar?	↓	N	N	N	N	N	N	↓	CP right
N.	71	Vascular	Right	Medullar	↓	↓	N	N	N	N	N	N	CP left
P.	73	Vascular	Left	Pontine	↓	↓	N	↓	N	↓	↓	↓	DP right
R.	71	PSP	Bilateral	Supranuclear	↓	↓	N	↓	N	↓	↓	↓	CP right DP right
R.	58	Vascular	Right	Pontine	↓	↓	↓	N	N	↓	N	↓	CP left
S.	72	Vascular	Left	Lateromed	↓	↓	↓	N	N	↓	↓	↓	–
W.	46	Vascular	Right	Pontine	↓	↓	↓	N	N	↓	↓	↓	DP right

s possible at the light diodes. At least five accades were recorded for each angle and di-ection.

Caloric nystagmus was produced by a rou-ne caloric test with warm and cold water and ne test was conducted in darkness (Henriks-on et al., 1972).

Nystagmus caused by *rotation* was pro-uced in a chair that was accelerated with 2.1 ad s^{-2} within one second to a constant velo-ty of 2.1 rad s^{-1}. After one minute of rotation ne chair was decelerated. The nystagmus in ne per- and postrotatory responses were easured. The test was performed in darkness ith both eyes open.

To elicit *optokinetic* nystagmus an opto-inetic cylinder covering the whole visual field as rotated around the subject at a constant elocity of 1.6 rad s^{-1}.

Optovestibular nystagmus was achieved ith a standardized visual surrounding and the atient was again rotated, as in the rotation est, but now with eyes opened.

An electro-oculographic technique was sed. Horizontal eye movements were re-orded binocularly, vertical eye movements onocularly from both eyes. The recorder sed was an ink-jet ENG recorder (Mingo-raph M 81) with an upper cutt-off frequency f 15 Hz. The paper was fed at a speed of 100 mm s^{-1}. The calibrations at 0.35 and 1.05 r were done twice, at the beginning and in t middle of the test.

In the present study, the main interest w directed towards the peak velocities in t movements of the eye. Normal values for t peak velocities in fast eye movements (He riksson et al., 1980) and smooth pursuit e movements (Schalén, 1980) and describ elsewhere. A velocity outside 95 % confiden limit from the normal mean value was regard as pathological. Thus, in the smooth pursu the maximal velocity was estimated during t time the patient was following the target (i without superimposed saccades) (Schalé 1980). In the voluntary saccades and the fa phases of nystagmus the peak velocities we measured and arranged in six different grou according to the amplitudes (Henriksson et a 1980). In the slow phases of nystagmus t peak velocity was estimated at the culminati response.

RESULTS

The most characteristic finding was that patients had impaired ability to perfo smooth pursuits. The second most chara teristic finding was that 9 out of 10 patients h significantly decreased velocities in volunta

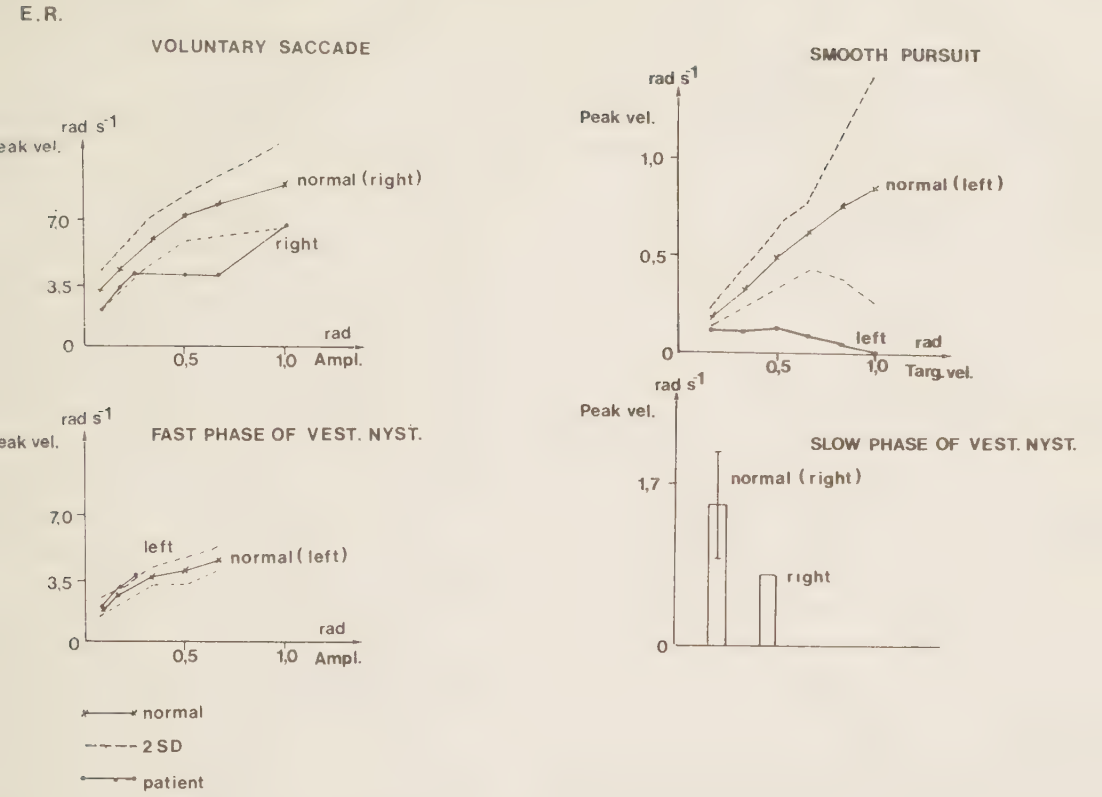


Fig. 1. Velocity patterns in voluntary saccades, smooth pursuits and fast and slow phases in angular acceleration induced nystagmus in a patient with PSP. Only eye movements to one side are depicted (the most pathological ones). Dashed lines indicate 2 S.D. on each side of the mean peak values in normals.

accades. The results are summarized in Table I.

In the rotation test the peak velocity in the st phase was significantly reduced in 6 out of) patients, the figures for optokinetic test and ptovestibular test being one out of 10 and 5 ut of 9, respectively.

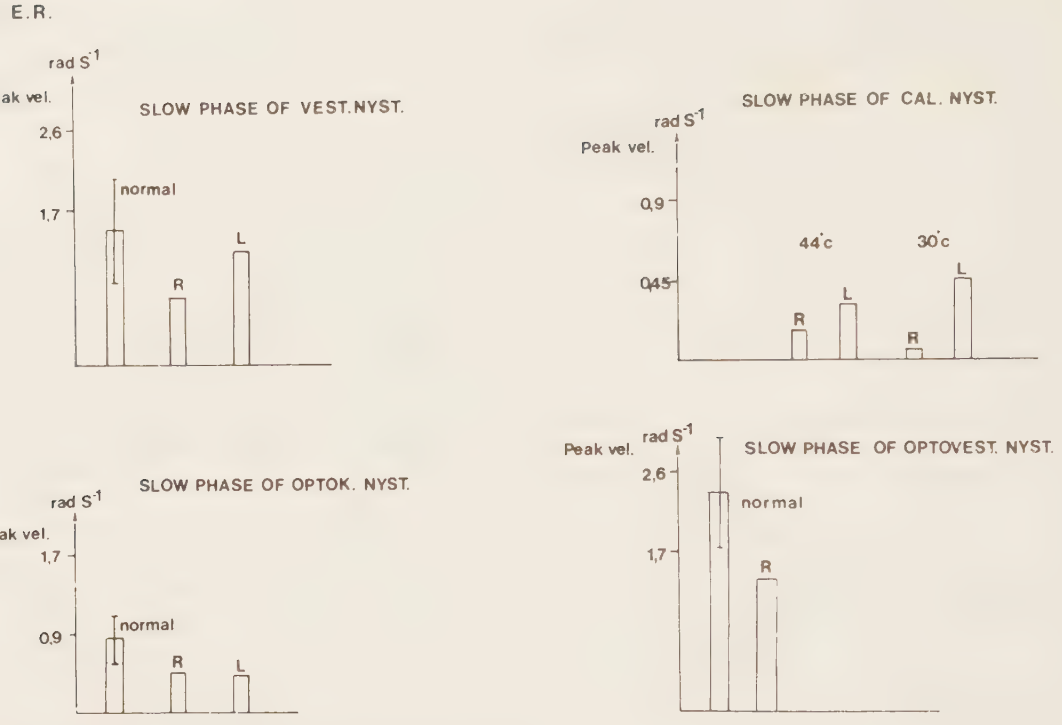
The most common abnormality in the slow hases was a decreased slow phase velocity in e optovestibular test (7 out of 9 patients). In e rotatory test 3 out of 10 were impaired and the optokinetic test 6 out of 10. Three paents had significantly decreased velocities in oth the rotation and the optokinetic test.

Sometimes, in the same individual, the velocty in one type of nystagmus could be normal, hile the velocity in the same component in her types of nystagmus was decreased Table I).

In caloric nystagmus the patients showed either directional preponderance (DP) or canal paresis (CP) and none had normal caloric responses. Four subjects had a DP and 6 had a CP. Four of the patients had a spontaneous nystagmus.

The findings in some of the patients are accounted for in detail in order to map out how various components of eye movements in the same individual are differently disturbed.

One patient (E. R.) had a progressive supranuclear palsy (Fig. 1). The pathological findings in this patient were decreased velocity in voluntary saccades as well as in smooth pursuits and slow phases of nystagmus in rotation test and optokinetic test, while the velocities of the fast phases in the same nystagmus were normal. In this patient the eye motor mechanism producing fast phases of nystagmus was



g. 2. Velocity patterns of slow components in different pes of nystagmus in the same patient as in Fig. 1. R= ght. L=left.

reserved, while the saccadic mechanism was sturbed, indicating a dissociation between accades and fast phases of nystagmus.

The slow phases in nystagmus in the same atient were affected in various ways (Fig. 2). he peak velocity of the slow phase of caloric ystagmus, of angular acceleration induced ystagmus and of optovestibular nystagmus as always reduced when directed towards ne right, while the optokinetic responses were educed in both directions. Thus, a dissocia- on between vestibular and optokinetic slow hases had taken place.

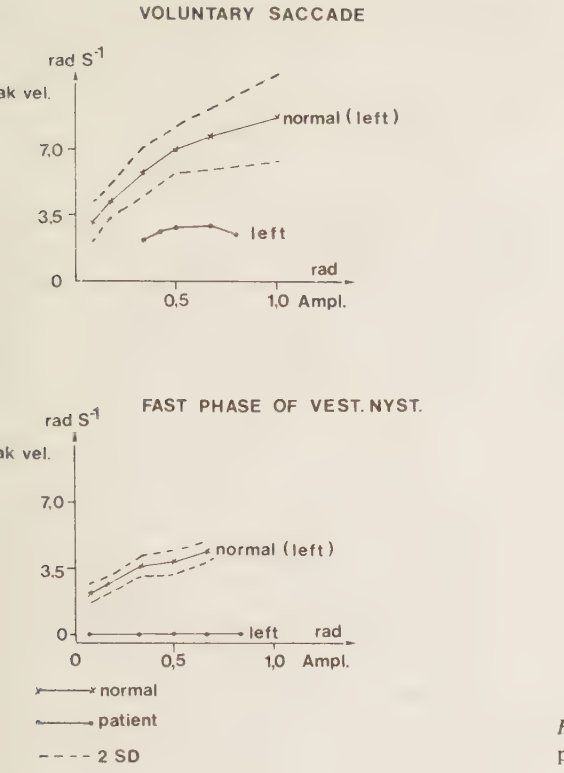
Another patient, a male with a tumour in the ourth ventricle (B. A.), had a markedly re- uced saccadic velocity (Fig. 3). For example, ith 0.7 rad amplitude the velocity was only 2 ad s^{-1} (normally 7.5 rad s^{-1}). During smooth ursuits his eyes lagged behind the target at arget velocities between 0.17–0.6 rad s^{-1}. lowever, at higher target velocities the smooth pursuits were within normal range and could not then be distinguished from the saccadic return eye movements (Fig. 4), because of almost identical shape and velocity. The dissociations in this patient are reflected by the presence of voluntary eye movements while the nystagmus was completely absent.

A third patient (E. J.) had an infarction in the brainstem (Fig. 5). She had normal velocities in both components in the rotatory test as well as in voluntary saccades. However, the ability to follow voluntarily was diminished, indicating a dissociation between mechanisms regulating the two types of voluntary eye movement (voluntary saccades and smooth pursuits).

DISCUSSION

The reason for selecting the peak velocity as the best parameter in discriminating betwee

B. A.



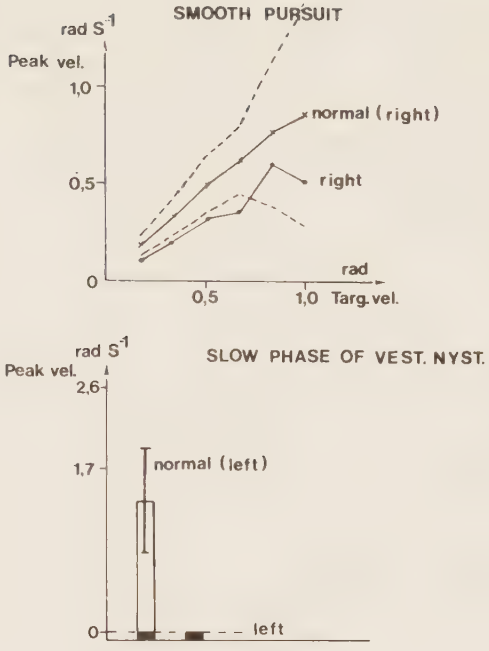


Fig. 3. Velocity patterns of different eye movements in a patient with a brainstem tumour.

althy and diseased subjects may need some planation. In the smooth pursuits the ability hold the object constantly in the fovea is flected by the maximal velocity (Robinson, 65). A normal peak velocity in the saccades d fast phases of nystagmus indicates intact nchronous firing of the neurons which trig-ger the right amplitude (Keller, 1974). The peak velocity in the slow phase of nystagmus measures the maximal gain in the vestibulo-ocular reflex arch (Melvill Jones & Milsum, 1971). Furthermore, the velocity parameter seems to be coded in pontine neurons (Keller, 1974).

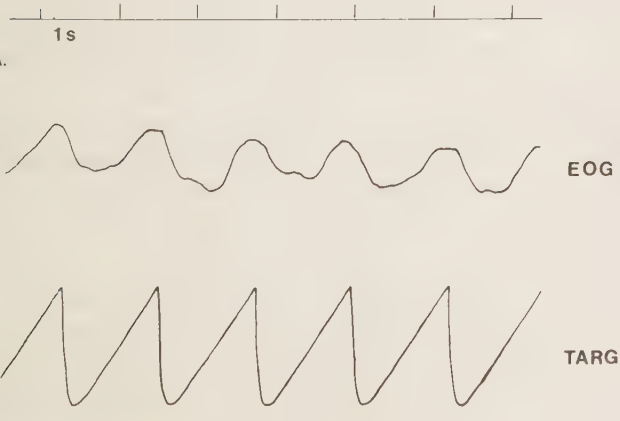


Fig. 4. EOG recordings of pursuit eye movements in the same patient as in Fig. 3.

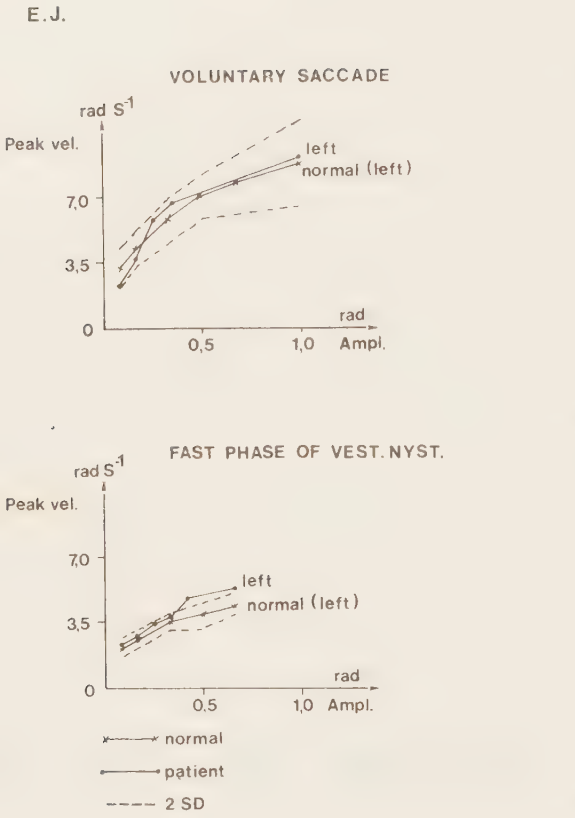


Fig. 5. Velocity patterns of different eye movements i patient with a brainstem infarction.

The velocity of the two types of voluntary eye movement was the most sensitive indicator of a pathological process in the pons. This is consistent with findings by other investigators (Baloh et al., 1975, 1977). The smooth pursuits, however, are disturbed in the same way in other neurological disorders, such as cerebellar lesions (Baloh et al., 1977) and cortical lesions (Hoyt & Daroff, 1971; Sharpe et al., 1979).

In the same way the voluntary saccades may be more sensitive than reflexive eye movements because of longer pathways and presumably a larger number of synapses. Certainly we also have to consider the difference in the interaction between the agonist and the antagonist in the different types of eye movements (Shimazu, 1972). According to previous experimental findings in animals (Keller, 1974) the same units in PPRF are active during all fast eye movements, whether voluntary sa cades or fast phases of nystagmus. Thus, could be expected that in a brainstem lesion fast eye movements would be equally affecte As the voluntary saccades in this study we more seriously disturbed than the fast phas of nystagmus, this model of eye motor fun tion cannot explain the present findings. difference in the neuronal organization of v luntary saccades and fast phases of nystagm is supported by previous findings in huma (Henriksson et al., 1980), where it was co cluded that the peak velocity in volunta saccades were faster than the peak velocity the fast phases of nystagmus.

Just as the peak velocity in voluntary sa cades and fast phases of vestibular nystagm could be unequally affected, the peak veloc in the fast phases of optokinetic nystagmus optovestibular nystagmus could be norm

hile the peak velocities in the corresponding hases of other types of nystagmus could be ignificantly decreased.

Similar differentially disturbed peak velo- ities were found in the slow phases of various ypes of nystagmus.

The velocity patterns of different eye move- ents described in the present study indicate neuronal organization at the pontine level, ossibly in the PPRF, different for all eye ovements. The findings might also help to nterpret and understand how normal eye ovements are brought about.

ZUSAMMENFASSUNG

ie Augenbewegungen von zehn Patienten mit Hirn- ammläsionen wurden mittels Elektro-okulografischer echnik untersucht. Eine Analyse der maximalen Ge- hwindigkeit in Blickfolge, Sackaden, per- und post- otatorischer Nystagmus, optokinetischer Nystagmus, ptovestibulärer Nystagmus und kalorischer Nystagmus urde ausgeführt. Die Resultate wurden mit der maxi- alen Geschwindigkeit der Augenbewegungen bei zwan- g Normalpersonen verglichen. In der Gruppe der Pa- enten mit Hirnstammsläsionen fielen ein oder auch ehrere Augenbewegungsteste bei dem einzelnen atienten pathologisch aus. In der gesamten Gruppe aren die voluntären Augenbewegungen verwundbarer s die reflexiven. Nach dem Blickfolgetest und dem oluntären Sackadentest ist der optovestibuläre Test am esten geeignet, wenn man Patienten mit Hirnstamms- sionen von Normalpersonen unterscheiden will.

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EYE-VELOCITY PROGRAMMING IN BRAIN-STEM DISORDERS

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INTRODUCTION

Visual illusions and vertigo are common symptoms in patients with brain-stem disorders.[1] Although many patients with brain-stem disorders do not have the above-described symptoms, an analysis of visually or vestibularly evoked eye movements may provide important information.[2-4]

There is experimental and clinical evidence that the immediate supranuclear center for upward gaze is located in the pretectum while the corresponding center for downward gaze is located more ventrally in the mesencephalic tegmentum.[5-7] This suggests two separate areas for upward and downward gaze.

The corresponding centers for horizontal eye movements are located in the pons, in the paramedian pontine reticular formation (PPRF). Units for rapid eye movements are located in the rostral parts, while units for slow eye movements are located more caudally.[8-10] These findings suggest separate mechanisms for rapid and slow eye movements.

In a previous study in patients with brain-stem lesions we found that saccades and smooth pursuit generally are more vulnerable than the quick and slow phases of nystagmus.[4] The above-described observations suggest separate mechanisms for voluntary eye movements and nystagmus.

Hence it can be expected that patients with disorders at different sites in the brain stem may present various patterns in their eye-movement disturbances.

The purpose of this paper is to find out how lesions at different levels in the brain stem affect eye--velocity programming.

MATERIAL

Thirty patients with lesions in the brain stem were referred to us by the Department of Neurology for electro-oculographical analysis. In the workup were included otoneurological and neuro-ophthalmological examination and axial computerized tomography. Mean age of the patients was 63 years (range, 17-81). The duration of the symptoms averaged 13 months with a wide range of 1 week to 12 years.

Twenty normal subjects with no history of vestibular or central nervous disease were used as controls. No drugs were allowed before the testing. Mean age of the controls was 48 years (range, 23-72).

In order to interpret the results, the patients were divided into three different groups according to the clinical findings, indicating at which level of the brain stem the lesions were located. (1) Five patients with progressive supranuclear palsy (PSP) - a degenerative disease with maximum pathological abnormality in the rostral parts of the brain stem. This group consisted of patients at different stages of the disease. (2) Fifteen patients with pontine disorders. This group consisted of 11 cases with infarctions, 3 cases with tumors, and 1 case with encephalitis. (3) Ten patients with lesions in the medulla oblongata. Eight of these cases had infarctions in the lateral medullary area, and 2 had medullary infarctions.

TEST PROCEDURE

The testing procedures were similar to those reported in earlier studies.[4,11,12]

The subjects were placed in a chair with occipital support for head stabilization. The eye movements were recorded by direct-current (d.c.) electro--oculography in a manner previously described for this laboratory.[11,12] To avoid errors due to filter effects, an analysis was made of the influence of different filters on the velocity patterns of different eye movements before the selection of the low-pass filter of 15 Hz was made.[11] Calibrations were checked twice, once before and once in the middle of the test.

Our interest was directed toward the velocity patterns of eye movements and, to a lesser degree, the accuracy of voluntary saccades and the number of superimposed saccades in the smooth pursuit.

The following eye movements were analyzed:

Smooth pursuit was induced by telling the patient to watch a light spot, 30 mm in diameter, projected on a screen 160 cm in front of the subject. The target was driven in predictable ramps of 60° amplitude at six different target velocities from 10° to 60°.

Voluntary saccades were induced by asking the patients to make rapid refixations between two targets, 5°, 10°, 20°, 30°, 40°, and 60° apart.

Rotatory responses were produced by rotating the subjects in a revolving chair at a rate of 120° for 60 seconds, following which the chair was decelerated within 1 second. The nystagmus was recorded in darkness.

Optokinetic responses (OKN) were induced by rotating a striped cylinder around the subjects with a speed of 90^{o}/second.

Optovestibular responses were produced by rotating the patient as in the rotation test but now inside the striped cylinder with open eyes in light.

RESULTS

Smooth pursuit

All patients but two showed severe impairments in the maximum velocities of the smooth pursuit. In FIGURE 1 is depicted the mean of the maximum smooth-pursuit velocities in the three groups of patients. There was no significant difference between the pontine and the medullary group. The PSP group, however, had significantly slower smooth pursuit than did the pontine and medullary patients ($p < 0.05$, Student's t-test).

A reduced velocity in smooth pursuit frequently, but not always, was accompanied by an increased number of superimposed saccades. An increased number of superimposed saccades (above mean, + 2 standard deviation in normal subjects) were found in all the patients with PSP, in 9 of the 15 patients with pontine lesions, and in 8 of the 10 patients in the medullary group.

Voluntary saccades

All patients with PSP and pontine disorders had a significantly reduced velocity in the voluntary saccades (below mean, - 2 SD in normal subjects). In the medullary group, however, this was found in 6 of the 10 patients. FIGURE 2 shows the mean values of the saccadic velocity at different amplitudes in the three groups of patients. There were significant differences in the velocities between the groups and also between each of the different groups and the normals ($p < 0.05$).

The accuracy of voluntary saccades, expressed as the amplitude of the initial saccade, was impaired significantly in all patients with PSP, in 10 of the 15 patients with pontine lesions, and in 3 of the 10 patients with medullary lesions.

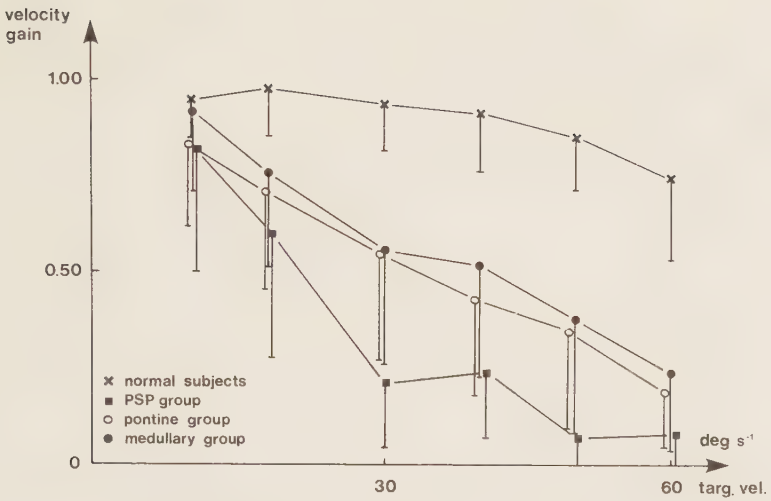

Fig. 1. Curves of maximum velocity gain in smooth pursuit of 20 normal subjects and of three groups of patients at different target velocities. The mean values with spreads (1 SD) of each group and at each velocity of the target are depicted.

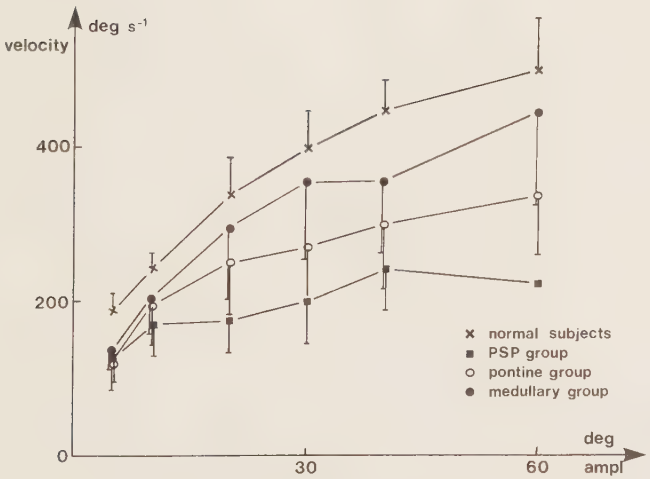

Fig. 2. Peak velocity-amplitude relationship of voluntary saccades in three groups of patients and in normal subjects. The mean values in each group at different amplitudes with 1 SD are depicted.

Nystagmus responses in the rotation test

The fast-phase velocity was reduced significantly in 1 patient of the 5 PSP patients tested, in 7 of the 15 patients with pontine disorders, but in only 1 of the 10 medullary patients tested. One patient with a medullary lesion even had a significantly increased velocity. In FIGURE 3 is depicted the mean of the fast-phase velocities in patients and normal subjects. The means of the fast-phase velocities in medullary patients at amplitudes of 30° and 40° were increased significantly compared to normal subjects ($p < 0.05$).

The maximum velocity in the slow component was reduced significantly in 3 of the 5 PSP patients, in 6 of the 15 patients with pontine lesions, and in 2 of the 10 patients with medullary lesions (FIGURE 4).

Nystagmus responses in the optokinetic test

The velocity of the fast component was reduced significantly in 1 of the 5 patients in the PSP group and in 2 of the 15 patients with pontine disorders, but was normal in all medullary patients except 3, who even had significantly increased velocities. In FIGURE 5 is shown the mean of the velocities of the fast component in patients and normal subjects. The medullary group had significantly increased velocities compared to normal subjects ($p < 0.01$) at an amplitude of 20°, while the PSP group had significantly reduced velocities ($p < 0.05$).

The maximum slow-phase velocity was reduced in all PSP patients, in 10 of the 15 patients with pontine lesions, and in 2 of the 10 patients with medullary lesions (FIGURE 6).

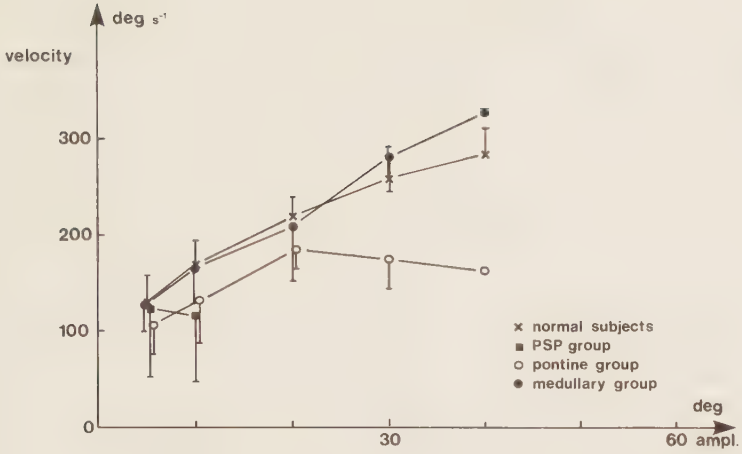

Fig. 3. Velocity patterns of fast phases of nystagmus in the rotatory test in normal subjects and the three groups of patients. Means and spreads as in Fig. 2.

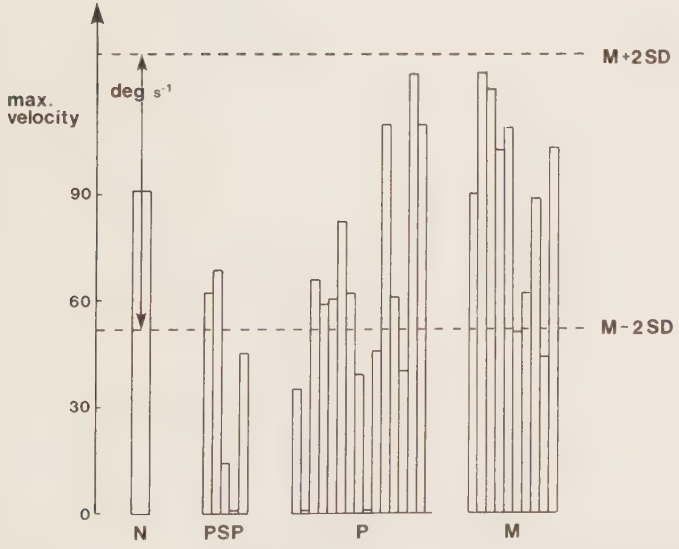

Fig. 4. Maximum slow-phase velocities in the three groups of patients are compared with the mean of the maximum slow-phase velocities in 20 normal subjects. Each patient is represented individually. Dashed lines indicate 2 SD above and below the mean values in normal subjects. N: mean values in 20 normal subjects. PSP: patients with progressive supranuclear palsy. P: patients with pontine disorders. M: patients with medullary and lateral medullary disorders.

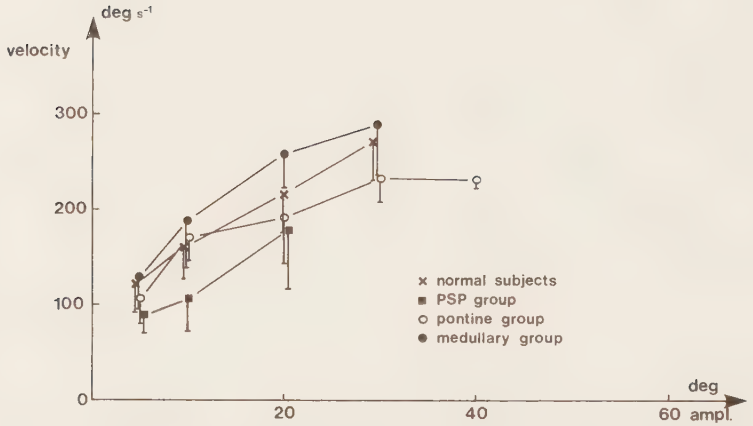

Fig. 5. Velocity patterns of the fast phases of OKN in normal subjects and in patients. Means and spreads as in Fig. 2.

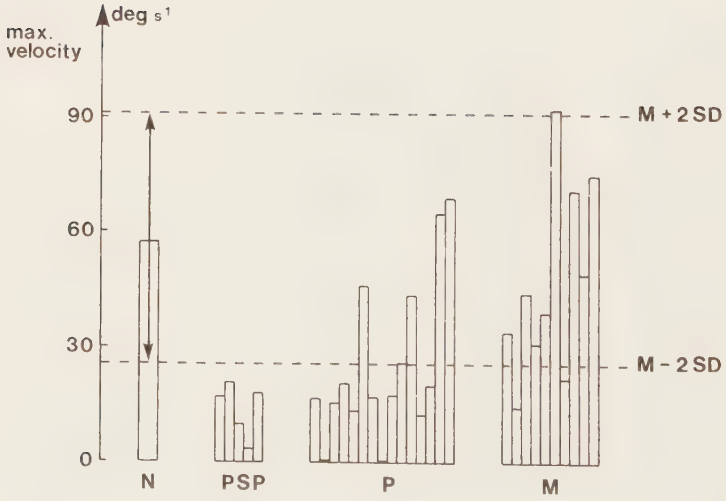

Fig. 6. Maximum slow-phase velocities in the OKN test. Abbreviations as in Fig. 4.

The velocity of the fast component was reduced significantly in 3 of the 4 patients with PSP, in 8 of the 12 (3 were not tested) patients with pontine lesions, and in 2 of the 9 patients with medullary lesions. In FIGURE 7 is depicted the mean of the fast-phase velocities in patients and normal subjects. All groups except the medullary group differ significantly from normal subjects ($p < 0.01$).

The slow-phase velocity was below the normal in 4 out of 4 (1 was not tested) patients with PSP, in 9 out of 12 patients with pontine lesions, and in 3 out of 9 patients with medullary lesions (FIGURE 8).

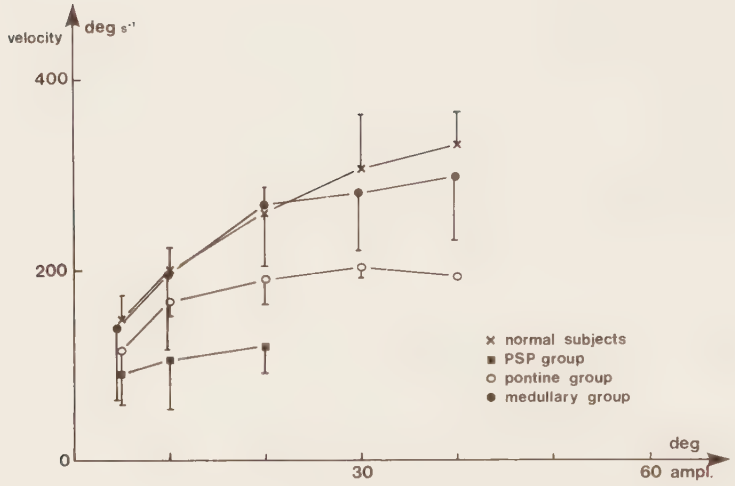

Fig. 7. Velocity patterns of the fast phases in the optovestibular test. Means and spreads as in Fig. 2.

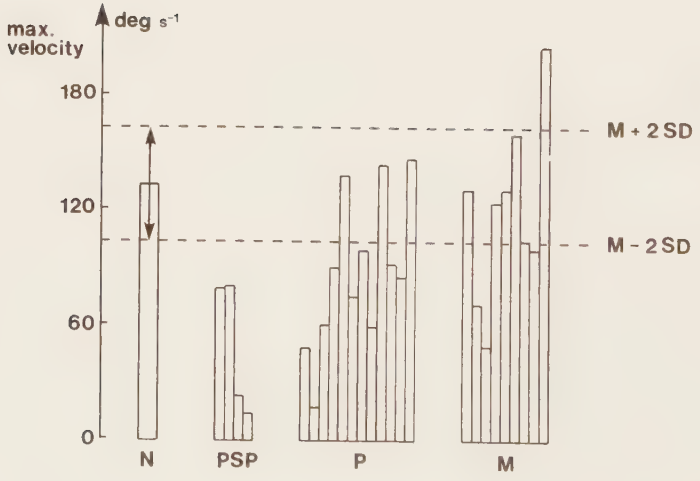

Fig. 8. Maximum slow-phase velocities in the optovestibular test. Abbreviations as in Fig. 4.

DISCUSSION

The electro-oculographic findings described in the present series of 30 patients with brain-stem lesions have confirmed the results of previous studies and have added to our knowledge of the characteristics of lesions at different sites in the brain stem.[2-4]

The maximum smooth-pursuit velocity was reduced uniformly in all cases but two, independent of the site of the lesion. Defective smooth pursuit in cases with lateral medullary lesions, as we have shown in the present paper, had been reported earlier by Hörnsten, Kommerell and Hoyt, and Pyykkö and Wennmo.[13-15] It is, however, not immediately obvious why patients with infarctions in the medulla should have disturbances of smooth pursuit, since the site of the lesion in many of our cases might be below the level of the PPRF. Nevertheless experiments on rabbits may be of relevance to the present findings because they support the assumption that afferent cerebellar visual fibers via the inferior olive are of importance in performing smooth pursuit.[16] Hence it is reasonable to assume that malfunctioning of these fibers may be a contributory factor to the abnormal smooth pursuit in cases of medullary lesions.

All cases with lesions in the rostral and intermediate parts of the brain stem had reduced velocities of voluntary saccades, while patients with lesions in the medulla frequently had normal saccadic velocities. Our findings are consistent with the notion that rapid eye movements, such as voluntary saccades, are integrated more rostrally in the brain stem than are slow eye movements.[8-10] Our results, however, somewhat contradict the results of Baker et al., who found units in the medulla with activity correlated not only to eye position but also to saccadic velocity.[17]

Both components in any type of nystagmus were preserved more frequently than were the voluntary saccades and the smooth pursuit, as pointed out in a previous study.[4]

Among the various types of nystagmus studied, the optovestibular type most frequently was liable to functional decline, possibly because of the need for two different sources of impulses.

The findings of preserved optokinetic slow phases in medullary and lateral medullary lesions in contrast to highly impaired smooth pursuit indicate that these two types of visually induced eye movements use different mechanisms. In testing OKN, we rotated the drum at a rather high speed (90°/second) and the patient had no possibility of fixating. Hence it was mainly the reflexive type of OKN that was tested.[18] Pathways relaying this type of OKN may reach directly the phasic units in the rostral parts of the pons from subcortical areas.[19,20] As patients with medullary disorders have their lesion below the level of the PPRF, this neuronal organization can explain why the OKN slow phases are preserved more commonly in medullary lesions than in pontine disorders and in patients with progressive supranuclear palsy.

In contrast to the optovestibular nystagmus, where both components were disturbed to about the same extent, the slow-phase velocity in OKN was reduced much more often than was the fast-phase velocity. This preservation and even enhancement of the fast-phase velocity in OKN as well as in postrotatory nystagmus, particularly in medullary lesions, may be due to the interruption of the cerebellar control of the PPRF, where all fast phases are supposed to be triggered.[10,21] This is in agreement with earlier observations of enhancement of the fast-phase velocity in patients with cerebellar lesions.[18]

Our findings indicate that an analysis of eye-movement velocities may provide important information on the localization of a brain-stem disorder. As computerized axial tomography of lesions in the posterior fossa has a high incidence of false-negative answers, the results of this type of electro-oculographical analysis may supplement radiological diagnosis of lesions in this area.

The relation between the site of a lesion and the preservation of some eye movements and disturbance of others also may be used for completing our understanding of normal eye motor processing.

SUMMARY

Eye movements in 30 patients with brain-stem lesions were evaluated with electro-oculography, and the findings were analyzed with regard to the site of the lesion in the brain stem. Eye velocities generally were reduced more severely in pontine than in medullary lesions. In medullary lesions, there even was a slight enhancement of the velocities in the fast component of optokinetic and postrotatory nystagmus. In contrast to the slow-phase velocity of OKN, which often was preserved in medullary lesions, the smooth-pursuit velocity was reduced in lesions at all levels in the brain stem. This indicates that these two types of visually induced eye movements use different mechanisms.

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EYE MOVEMENTS IN CEREBELLAR AND COMBINED CEREBELLO-BRAINSTEM DISEASES

By

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ABSTRACT

We report a quantitative analysis of eye movement disturbances in patients with isolated cerebellar disorders and patients with cerebellar disorders and concomitant brainstem involvement. The most characteristic abnormalities in the exclusively cerebellar patients were increased velocities of the slow phases of vestibular nystagmus induced by rotation in the dark and increased peak velocities of the fast phases of optokinetic nystagmus induced by fullfield optokinetic stimuli. Dysmetria of saccades was found in 3 of 6 cerebellar patients and gaze nystagmus in all these 6 patients. The typical findings in the combined cerebello-brainstem group were reduced peak velocities of voluntary saccades, defective smooth pursuit and reduced peak velocities of the fast component of nystagmus during rotation in both the dark and light. All patients with combined cerebello-brainstem disorder had dysmetric voluntary saccades and gaze nystagmus. The numbers of superimposed saccades during smooth pursuit were uniformly increased.

Release of inhibition in cerebellar disorders may explain the hyperresponsiveness and inaccuracy of eye movements found in this study. In addition, when lesions also involve the brainstem, however, integrative centers coding eye velocity are affected leading to slow and inaccurate eye movements. These features elicited clinically may be useful in the diagnosis of cerebellar and brainstem disorders.

INTRODUCTION

Previous studies in patients with presumed cerebellar lesions have often failed to describe a consistent pattern of ocular motor abnormalities.[1,2] This inconsistency may have been due to the presence of lesions also involving the brainstem in some of the patients. Recently eye movement disorders in patients with presumed cerebellar atrophy have been reported.[3,4] It was not documented, however, whether the findings were similar in cerebellar disorders irrespective of etiology. Furthermore, except for voluntary saccades, no analysis of fast eye movements was made. As will be demonstrated in the present results, differences in fast phases of nystagmus can be just as indicative of a cerebellar lesion as those in slow phases of nystagmus.

In this study, we analyzed the patterns of the various types of eye movements in two groups of patients: the first with signs of cerebellar origin only, and the second with signs of both cerebellar and brainstem involvement. Firstly we hoped to distinguish these two groups of patients on the basis of characteristic differences in the oculomotor function and secondly we wanted to compare the vulnerability of different types of rapid eye movements.

MATERIAL AND METHODS

Each group consisted of 6 patients (Table I). The first group had exclusive signs of cerebellar involvement, while the other group exhibited cerebellar dysfunction combined with disorders of the cranial nerves and of sensory or pyramidal tracts, indicating involvement of brainstem structures (Table II). The diagnosis was confirmed by neurological work-up including neuro-ophthalmological examination and computerized axial tomography.

As controls, we used 20 normal persons without any history of vestibular or neurological disease, 10 males and 10 females. The mean age was 48 years (range 23 to 72). The age of the controls corresponded roughly to those of the diseased subjects set out in Table I.

Test procedure

Voluntary saccades were evoked by asking the patient to look alternatingly at light diodes located horizontally 0.08, 0.17, 0.35 and 0.59 rad on each side of the midline. At least five saccades were recorded for each angle and direction.

Smooth pursuit was evoked by telling the patient to track a light spot 30 mm in diameter, at a distance of 160 cm, moving at a constant velocity on a horizontal screen. The test was conducted at velocities of 0.17, 0.35, 0.52, 0.70, 0.87 and 1.05 rad s^{-1}. The test was performed both to the right and to the left. Five recordings were made in each direction and at each velocity.

Vestibular nystagmus was induced by rotating the subject in a chair accelerated within one second to a constant velocity of 2.1 rad s^{-1}. After rotation for

Table I. Diagnosis, age and duration of symptoms before the EOG recordings were performed in all the patients. C = Patients with cerebellar disorders. CP = Patients with cerebello-brainstem disorders.

PAT.	DIAGNOSIS	AGE	DURATION OF SYMPTOMS BEFORE EOG RECORDING
C			
E.A.	Infarction	49	2 weeks
G.C.	Atrophy	39	1½ year
S.E.	Atrophy	52	1 year
B.S.	Metastasis	50	1½ month
K.S.	Multiple sclerosis	53	2 months
M.T.	Hematoma	52	1½ week
CP			
C.M.	Degeneration	33	1 year
I.N.	Encephalitis	47	1 year
G.O.	Medulloblastoma	27	11 years
I.P.	Infarction	36	2 weeks
T.P.	Metastasis	69	1 year
E.S.	Ependymoma	33	2 years

Table II. Clinical signs indicating involvement of different structures.

	CRANIAL NERVES													
PAT.	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	PYRAMIDAL TRACTS	CEREBELLUM
E.A.														+
G.C.														+
S.E.														+
B.S.														+
K.S.														+
M.T.														+
C.M.													+	+
I.N.			+		+	+	+	+					+	+
G.O.									+	+				+
I.P.					+									+
T.P.												+		+
E.S.									+					+

one minute the chair was decelerated to a standstill within one second. The per- and postrotatory responses were measured.

Optokinetic nystagmus was induced by rotating, around the patient, a striped cylinder at a velocity of 1.6 rad s^{-1}.

Optovestibular nystagmus was evoked by rotating the patient, with eyes open, in the same way as in the rotation test but this time inside the striped cylinder.

Each patient was examined for spontaneous and gaze nystagmus, with eyes open in darkness during the electro-oculographic recordings and with Frenzel's glasses in light.

The eye movements were recorded with a DC electro--oculographic technique with infinite time constant and upper cut off frequency of 15 Hz. Horizontal eye movements were recorded bitemporally, and vertical eye movements were recorded monocularly. Standard electrodes (Medicotest) with jelly were used. The recorder was a DC-coupled ink-jet writer (Mingograph M 81, Siemens Elema, Stockholm, Sweden). Paper speed was 100 mm s^{-1}. Two calibration tests were made, one before and one in the middle of the test.

The main thrust of this study was to analyze velocities of voluntary saccades, smooth pursuits and velocities of the fast and slow components of vestibular, optokinetic and optovestibular nystagmus.

In addition, the accuracy of the saccades and the total number of superimposed saccades during smooth pursuit were measured.

Calculation and statistical evaluation

Peak velocity was measured from the recordings by handscoring and the data were calculated by computer (Univac-11-08-EXC-8). As the velocity of rapid eye movements is related to the amplitude, the peak velocities of the rapid eye movements were arranged in six different groups according to amplitude.[5,6] Maximum velocity of the slow component was measured at the response culmination. The maximum velocity of the smooth pursuit was measured during the time the patient was observing the target (the velocity of the superimposed saccades was not studied). The peak velocity of each type of eye movement for each patient was compared with the mean of the peak velocities in 20 normal subjects. Those velocities which fell outside 95 per cent confidence limit were regarded as pathological. The accuracy of the initial saccade, expressed by the amplitude, was compared to the mean value in 20 normal subjects at amplitudes of 0.35 and 1.05 rad. Values outside 2 SD from the mean value were regarded as pathological. The same evaluation was made for the total number of superimposed saccades during a constant period of eye tracking.

RESULTS

Voluntary saccades

The results obtained by analyzing the peak velocities of the voluntary saccades are shown in Figs. 1 and 2. In the cerebellar disorder group, reduced peak velocities were observed in one, normal peak velocities in 4, and increased peak velocities in one patient. In the cerebello-brainstem disorder group all patients displayed reduced peak velocities.

Inaccurate voluntary saccades, primarily hypometria, were found in 3 cerebellar patients. All 6 patients with cerebello-brainstem disorders showed dysmetric voluntary saccades.

Smooth pursuit

Figs. 3 and 4 exhibit individual maximum smooth pursuit velocity curves. In the cerebellar disorder group, smooth pursuit velocity was reduced in 2 and normal in 4 patients, while in the cerebello-brainstem disorder group, 5 subjects exhibited reduced smooth pursuit velocities and the velocity was normal in one.

The number of superimposed saccades was increased in 2 subjects in the cerebellar group. One of them had normal smooth pursuit velocity, while the second had significantly reduced velocity. The frequency of superimposed saccades in the cerebello-brainstem group was increased in 5 and normal in one patient.

Vestibular responses

Eye movements in response to rotational stimuli revealed pronounced differences between the two groups. In the cerebellar disorder group, the maximum velocity of slow phases of nystagmus (Fig. 5) was increased in

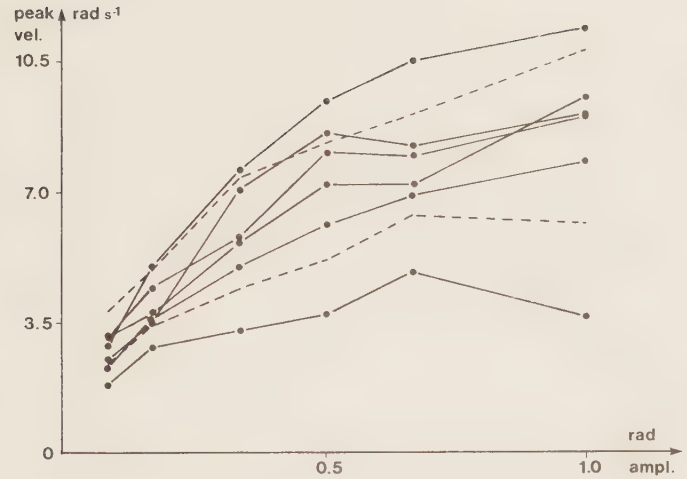

Fig. 1. Amplitude-peak velocity relationship of voluntary saccades in patients with cerebellar lesions. Each curve represents one individual. Dashed lines represent 2 SD on each side of the mean peak values in 20 normal subjects (Henriksson et al., 1980).

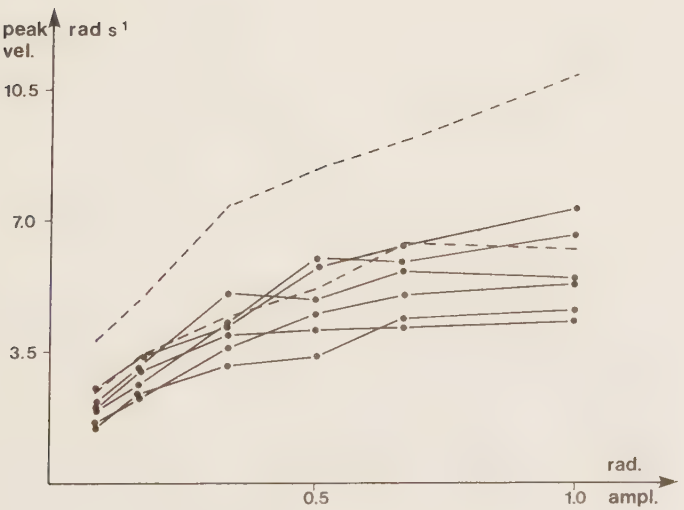

Fig. 2. Amplitude-peak velocity relationship of voluntary saccades in 6 patients with cerebello-brainstem disorders. Dashed lines as in Fig. 1.

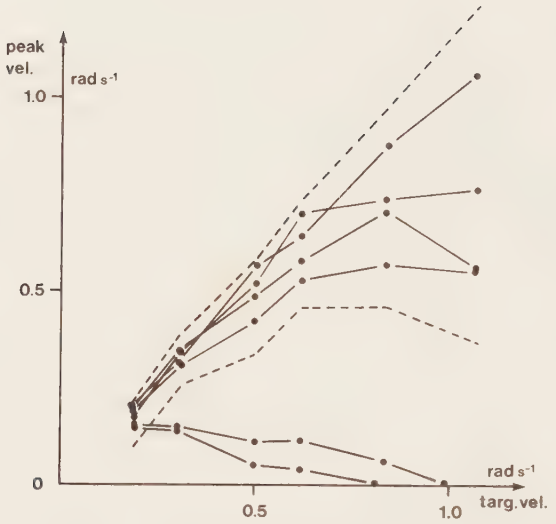

Fig. 3. Maximum velocities of smooth pursuit at different target velocities in 6 patients with cerebellar disorders. Dashed lines as in Fig. 1.

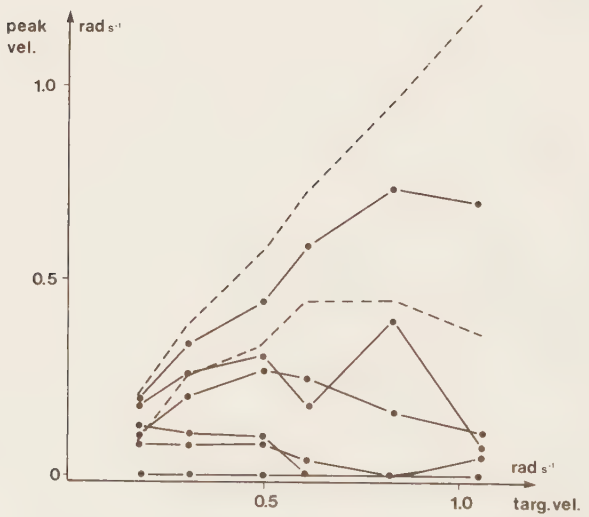

Fig. 4. Maximum velocities of smooth pursuit at different target velocities in 6 patients with cerebello-brainstem disorders. Dashed lines as in Fig. 1.

5 subjects and decreased in one, whereas in the cerebello-brainstem disorder group (Fig. 5) 2 subjects exhibited reduced velocity in the slow component of nystagmus and 4 were normal.

The peak velocity of fast phases of nystagmus in cerebellar patients (Fig. 6) was significantly increased in 3, within the normal range in 2 and significantly slow in one subject. However, in the cerebello-brainstem group, 5 patients presented abnormally slow peak velocities, while the velocity was increased in one patient (Fig. 7).

Optokinetic responses

In patients with cerebellar disorders, the slow component of optokinetic nystagmus was above the normal range in 2, within normal limits in 3, and below the normal range in one subject. In the patients with cerebello-brainstem disorders, the maximum velocity of the slow component of optokinetic nystagmus was normal in one and decreased in 5 subjects.

In the fast components of optokinetic nystagmus the peak velocities in cerebellar patients were increased in 5 subjects and normal in one, while in the cerebello-brainstem patients, the peak velocities of the fast component were normal in 2 and decreased in 4.

Optovestibular responses

All cerebellar patients who were tested (5/6) had normal peak velocities in the slow phases (Fig. 8). In the fast phases, 3 patients exhibited significantly increased velocities. In the cerebello-brainstem group, 3 patients had decreased velocities in both components, while 2 had decreased velocities only in the fast phase.

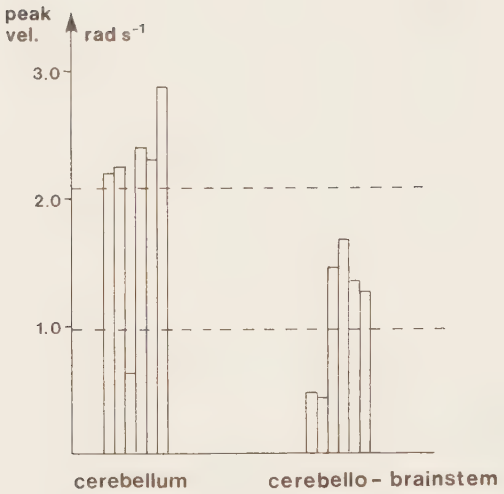

Fig. 5. Slow phase velocities at the culmination response of the post-rotatory reaction in patients with cerebellar and cerebello-brainstem disorders. Dashed lines as in Fig. 1.

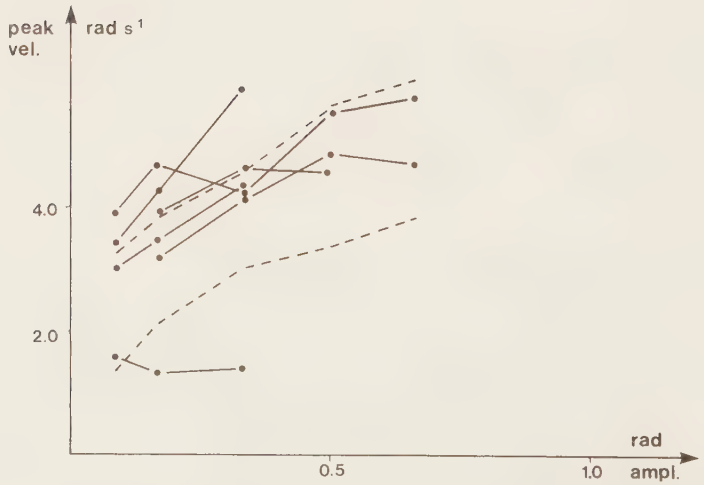

Fig. 6. Amplitude-peak velocity relationship of the fast phases in the rotatory test in cerebellar patients. Dashed lines as in Fig. 1.

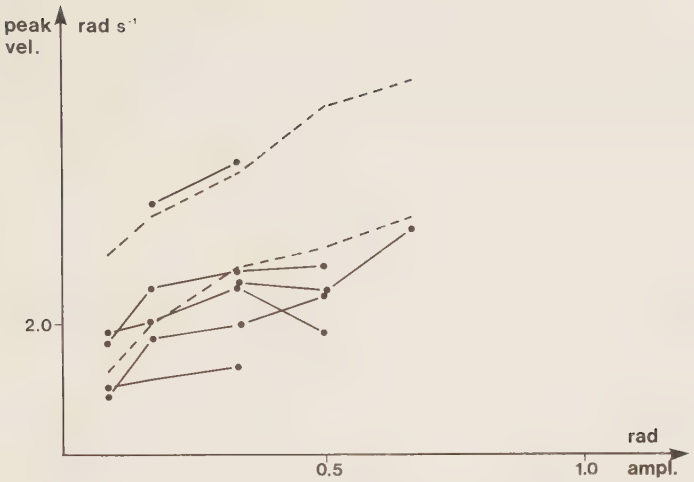

Fig. 7. Amplitude-peak velocity relationship of the fast phases in the rotatory test in cerebello-brainstem patients. Dashed lines as in Fig. 1.

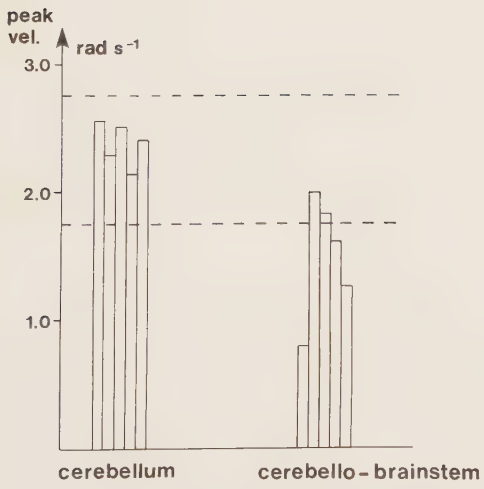

Fig. 8. Maximum slow phase velocities in the optovestibular test in patients with cerebellar and cerebello-brainstem disorders. Dashed lines as in Fig. 1.

Table III. A summary of the findings in all the different types of eye movements which were performed in the tests. Values outside 2 SD from the mean values in 20 normal subjects are regarded as pathological. N = normal; ↓ = decreased; ↑ = increased.

PAT.	TYPE OF LESION	PURSUIT VELOCITY	SACCADE VELOCITY	ROTATION FAST	ROTATION SLOW	OKN FAST	OKN SLOW	OPTOVEST. FAST	OPTOVEST. SLOW	DYSMETRIA	SUPERIMPOSED SACCADES
E.A.	Infarction	N	N	▲	▲	▲	▲	N	N	No	N
G.C.	Atrophy	N	▲	▲	▲	▲	▲	▲	N	No	N
S.E.	Atrophy	▼	N	N	▲	▲	▼	▲	N	Yes	▲
B.S.	Metastasis	N	N	▲	▲	▲	N	▲	N	Yes	N
K.S.	Multiple sclerosis	N	N	N	▲	▲	N	N	N	No	▲
M.T.	Hematoma	▼	▼	▼	▼	N	N	-	-	Yes	N
C.M.	Degeneration	N	▼	▼	▼	▼	▼	▼	▼	Yes	N
I.N.	Encephalitis	▼	▼	▲	▼	N	▼	-	-	Yes	▲
G.O.	Medullo-blastoma	▼	▼	▼	N	▼	▼	▼	N	Yes	▲
I.P.	Infarction	▼	▼	▼	N	N	N	▼	N	Yes	▲
T.P.	Metastasis	▼	▼	▼	N	▼	▼	▼	▼	Yes	▲
E.S.	Ependymoma	▼	▼	▼	N	▼	▼	▼	▼	Yes	▲

Table III is a summary of the findings in all types of eye movements.

Spontaneous and gaze nystagmus

In the cerebellar disorder group, 2 of the patients exhibited a horizontal spontaneous nystagmus, 5 had direction-changing gaze nystagmus, and one had direction-fixed gaze nystagmus. Downbeat nystagmus was observed in one patient.

In the cerebello-brainstem group, 3 subjects exhibited spontaneous nystagmus and all subjects demonstrated direction-changing gaze nystagmus.

DISCUSSION

The vestibulocerebellum and the dorsal and posterior vermis are particularly closely related to ocular motility.[7,8,9,10] These areas are known to receive afferent signals via visual and vestibular pathways.[11] Lesions of the dorsal vermis can cause saccadic instability,[12] while changes in smooth pursuit are found in cases of floccular process.[13,14]

Findings of increased velocities of the two types of rapid eye movement, voluntary saccades and fast phases of nystagmus (Table III), have not previously been reported in cerebellar lesions. Thus, in such cases, a normal amplitude-velocity relationship of voluntary saccades has been reported by Aschoff and Cohen,[7] Zee et al.,[4] and by Ellenberger, Keltner and Stroud,[15] while even reduced velocities were found by Baloh et al.[3] The conclusions drawn from our findings are supported to some extent by the observation of Ron and Robinson[16] who, by varying electrical stimulation of cerebellum, were able to provoke variations in saccadic velocity. It is not clear, however, how this velocity increase, as found in our study, can be explained. It may well indicate an increased frequency of spikes in neurons responsible for rapid eye movements, or a too early interruption of a saccade or quick phase preprogrammed to larger amplitudes. Some observations in animal experiments suggest the latter possibility.[16]

Inaccuracy of voluntary saccades is a phenomenon repeatedly found in patients with lesions of the cerebellum.[4,17] Both hypermetria and hypometria occur, even if hypometria is the more common[18] and is rather typical of vermal lesions.[7,12] Hypometria of saccades is a common finding in various brain disorders and a very striking inaccuracy of saccades has been found in patients with frontal lobe lesions.[19] In the

present study, inaccuracy of saccades, reflected overwhelmingly by hypometria, was more frequently found in patients with cerebello-brainstem lesions than in patients with cerebellar lesions.

The velocity of smooth pursuit was decreased in 2 out of 6 patients with cerebellar disorders. Baloh et al.[3] and Zee et al.[4] frequently found impaired smooth pursuit in patients with cerebellar ataxia. The visual information for smooth pursuit is believed to be projected via the dorsal capsule of the inferior olive to the vestibulocerebellum.[20,21] Furthermore, selective lesions of the flocculus in the monkey impair the ability for smooth tracking.[14] In hereditary cerebellar ataxia, cell degeneration occurs in the flocculus, the inferior olive and various cerebellar nuclei,[4] all structures possibly important for performing smooth pursuit. In the present study, some cerebellar patients had normal smooth pursuit, indicating that the floccular output was still adequate in these cases. Another possibility might be that the cerebellar dysfunction was compensated for by mechanisms elsewhere.[4] In contrast to this normal smooth pursuit, 5 out of 6 patients with cerebello--brainstem lesions showed a reduced smooth pursuit velocity. It must therefore be expected that in the brainstem, structures involved in performing smooth pursuit are very sensitive to lesions, as was also indicated in a previous study.[22]

Low velocity in smooth pursuit affected by cerebello--brainstem lesions was compensated for by superimposed saccades. In one of the patients with a cerebellar disorder we found normal smooth pursuit velocity, and in spite of this an increased number of superimposed saccades. Thus, a higher readiness for saccadic release was present than was needed in order to assist the smooth pursuit system. However, in the majority of the patients with cerebellar disorders, superimposed saccades compensated for a low smooth pursuit gain.

The inhibitory effect of the cerebellum as exerted on the vestibular nuclei[23] provides an explanation for the changes in the velocity of the nystagmic slow component. Moreover, Ito, Nisimaru and Yamamoto[24] showed that electrical stimulation of the flocculus causes increased inhibition of the ipsilateral vestibular nucleus and hence a diminished horizontal canal reflex. Furthermore, Takemori and Suzuki[25] observed that lesions of the deep cerebellar nuclei, responsible for relaying the major output from the cerebellar cortex, lead to a marked increase in the velocity and duration of caloric nystagmus. In cerebellar lesions, loss of inhibition of the neuronal activity initiated by the horizontal canal system[23] could thus explain the present findings of vestibular hyperactivity in patients with cerebellar disorders.

Several reports have dealt with optokinetic nystagmus in experimental cerebellar lesions. In foveate animals, the optokinetic slow phase consists of two portions.[26,27] The initial rise, characterized by an immediate increase in velocity of the optokinetic nystagmus, is followed by a slow rise, consisting of accumulations of velocity increments.[27] The former is believed to use smooth pursuit mechanisms and the latter, vestibular mechanisms.[28,29] In non-foveate animals, like rabbits,[30] ablation of the cerebellum has little effect on the slow phase velocity of optokinetic nystagmus, indicating that optokinetic engagement via vestibular pathways is not dependent on the cerebellum. In foveate mammals, as in monkeys[14] or in human beings,[31] cerebellar lesions lead to a decrease in slow phase velocity, its time constant being prolonged together with a reduced gain. This indicates that optokinetic nystagmus using smooth pursuit mechanisms is dependent on cerebellar function.

When in the optokinetic test the optokinetic drum is operated at high velocities (1.57 rad s^{-1}), the patient is quite unable to fixate.[32] Therefore, it is

mainly the reflexive type of optokinetic nystagmus which is tested.[33] This can explain why the optokinetic responses could remain intact in cerebellar lesions and even be enhanced in much the same way as the slow component of vestibular nystagmus.

The velocity of the slow component of optovestibular nystagmus was normal in all the subjects with cerebellar disorders, while it was decreased in all but two subjects with cerebello-brainstem lesions. The reason for the normal values could be: (1) co-operation between the visual and the vestibular system compensating for defects in optokinetic and vestibular nystagmus, or (2) hyperactivity in the vestibular response, restoring the reduced optokinetic response.

CONCLUSIONS

In spite of the diversity of the results in the different tests, they are connected by a thread of consistency that seems to suggest a constellation that is unique to a cerebellar disorder compared with a cerebello-brainstem disorder.

It seems possible to distinguish a cerebellar lesion from one that involves the brainstem, on the following basis: "Pure" cerebellar patients generally show: (1) increased or normal peak velocities of voluntary saccades, while the cerebello-brainstem patients have decreased velocities; (2) increased or normal responses of the maximum velocity in the fast and/or slow component of vestibular nystagmus, compared with decreased or normal velocities in cerebello-brainstem patients; (3) increased or normal peak velocities in the fast component in optokinetic nystagmus, whereas decreased or normal velocities in the same type of nystagmus are found in cerebello-brainstem patients; (4) increased or normal peak velocities in the fast phase of the optovestibular test compared with decreased velocities in the cerebello-brainstem group.

In the same way it would seem possible to distinguish a patient with a cerebellar lesion from a normal person, on the following basis: (1) inaccuracy of voluntary saccades, (2) defective smooth pursuit, (3) increased peak velocities in the fast and/or slow component in the rotatory test, (4) increased peak velocities in the fast component of optokinetic nystagmus, and (5) inability to hold excentric gaze.

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VESTIBULAR NEURONITIS

A Clinical and Electro-oculographic Analysis

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bstract. Thirty patients, primarily diagnosed as having estibular neuronitis, were investigated with a test battery nsisting of neuro-otological, neuro-ophthalmological, urological examinations and electro-oculography. Ini- l routine examination failed to reveal involvement of ructures outside the vestibular nerve, whereas neuro- gical evaluation and analysis of the cerebrospinal fluid dicated an intrinsic central nervous system (CNS) disor- r in 6 cases. The electro-oculographic analysis revealed normalities supporting a 'central' cause of the vertigo in cases. Altogether 13 patients showed signs of a possi- e intrinsic CNS disorder. Consequently, although rou- ne examination may indicate a diagnosis of vestibular uronitis, the patient concerned frequently has signs of intrinsic CNS disorder and not a disorder of the periph- al nerve.

he etiology of vestibular neuronitis is un- nown, but the disorder has been linked to euronitis of the vestibular nerve caused by fection (Dix & Hallpike, 1952; Coats, 1969). ecause of the benign character of the disease nly a few cases have been examined at autop- (Lindsay & Hemenway, 1956; Schuknecht Kitamura, 1981). These reports show nerve ell degeneration of the peripheral nerve with tact or only partly degenerated end organ.

In clinical routine work, a single attack of ertigo perceived as a spinning sensation ound the head, and lasting for days or eeks, without concomitant hearing loss or eurological symptoms may indicate a diagno- s of vestibular neuronitis. This diagnosis is rther supported if unilateral (Lachman & ahle, 1967; Pfaltz & Meran, 1975) or even lateral weakness (Dix & Hallpike, 1952) is und in the caloric test. These two indica- ons of neuronitis of the vestibular nerve—the character of vertigo and a canal paresis in th caloric test—are, however, not exclusive sign of a peripheral vestibular disorder. Firstly, th vertigo of vestibular neuronitis cannot alway be distinguished from that of labyrinthine dis orders nor from vertigo due to disturbances o the central nervous system (Fisher, 1967) Secondly, the caloric test may not reliabl separate central and peripheral vestibular dis orders (Baloh et al., 1977 *b*; Wennmo & Hind felt, 1980).

The purpose of our investigation was t look for signs of an intrinsic central nervou system (CNS) disorder in cases interpreted a having vestibular neuronitis when routinel examined. This intention was carried ou firstly, by a quantitative analysis of voluntar and involuntary eye movements and, second ly, by neurological examination including i some cases an analysis of the cerebrospina fluid.

MATERIAL AND METHODS

Thirty consecutive patients, 14 men and 1 women, whose ages ranged from 23 to 6 (mean 51.9 years), were included in the study Electro-oculographic (EOG) and audiologica tests were run on all patients and careful neu rological and neuro-ophthalmological exam nations were performed, including in 9 case analysis of the cerebrospinal fluid.

Twenty healthy subjects were used as con trols. These were 10 men and 10 women, rang ing in age from 23 to 72 (mean 48 years) an

o had no history of misuse of drugs or ohol and no evidence of previous vestibular neurological disease.

Test procedure

ontaneous nystagmus, gaze nystagmus and *sitional nystagmus* were recorded in dark-ss with open eyes. Spontaneous nystagmus s measured with the subject in supine posi-n and with his eyes in neutral position. rizontal gaze nystagmus was measured h ocular deviation 30 deg from the neutral sition. Positional nystagmus was measured en the patient turned his head 90 deg to ch side.

The *caloric test* was performed in darkness h eyes open and with a water temperature 7°C below and above body temperature. e duration of the irrigation period was 20 s.

The *rotation test* was performed in total rkness with open eyes by accelerating the bject in one second to a constant velocity of 0 deg s^{-1}. After 1 min of rotation the chair s brought to a standstill within one second. e postrotatory responses in both directions re measured.

The *optokinetic test* was performed with the bject sitting inside a striped rotating cylin-r. The cylinder was accelerated to a con-nt velocity of 90 deg s^{-1} within 10 s.

The *optovestibular test* was performed by ating the subject inside the stationary opto-netic cylinder in light with open eyes.

Voluntary saccades were measured at an-s of 5, 10, 20, 30, 40 and 60 deg. The subject s asked to switch his gaze rapidly between o light diodes placed horizontally at a dis-nce of 120 cm in front of his eyes. Ten ccades were analysed for each angle and ection.

Smooth pursuit was recorded when the pa-nt with his eyes pursued a target moving at nstant velocities of 10, 20, 30, 40, 50 and 60 g s^{-1}. Five consecutive eye movements at ch velocity to the right and left were record-and analysed.

The eye movements were recorded with a d.c. oculographic technique with infinite tim constant and an upper cut off filter of 15 Hz The recorder was a d.c. coupled ink-jet write (Mingograph M 81, Siemens Elema, Stock holm, Sweden). Horizontal eye movement were recorded bitemporally and vertical ey movements were recorded monocularly.

Calculation from the recordings

From the EOG recordings we measured th maximum velocity at response culmination o the slow components of caloric, post-rotatory optokinetic (OKN) and optovestibular nystag mus and the peak velocity in voluntary sac cades and maximum velocity of smooth pu suit. The main parts of the methods have bee described previously (Henriksson et al., 198 Schalén, 1980; Wennmo & Hindfelt, 1980). I the tests which induced nystagmus we looke for reduced responses and direction preponderance. Furthermore, the occurrenc of spontaneous nystagmus, gaze nystagmu and positional nystagmus was noted.

Normal distributions

Normal values for maximum slow phase ve locity calculated from 20 healthy subject were as follows (mean and standard dev ations): In the rotation test 91±16.5 deg s^{-} in the optokinetic test 58±16.4 deg s^{-1}, and i the optovestibular test 133±14.9 deg s^{-} Those velocities which fell outside 95% conf dence limit were regarded as pathological.

To count smooth pursuit and voluntary sac cades as pathological we required values ou side the normal area (mean ±2 SD) for at lea two of six target velocities in the smooth pu suit test and two of six tested amplitudes the saccade test. Normal values for direction preponderance (DP) were calculated on th basis of the formula Cvr−Cvl/Cvr+Cvl (Jon kees & Philipszoon, 1963), where Cvr and C are the maximum velocities at culmination r sponse to right and left. In the rotation te normal values for DP were 0.02±0.12 and the optokinetic test 0.01±0.16. The optove tibular test was performed in one directio

ble I. *Total number of patients with spontaous, gaze or positional nystagmus*
30.

	Spontan. nystag.	Gaze nystag.	Posit. nystag.
lateral	26	22	16
teral		4	5
	26	26	21

Table II. *Number of patients with reduced responses (hyporeflexia) and directional preponderance (DP) in the caloric, postrotatory, optokinetic and optovestibular tests*

Test	Hypo-reflexia	DP
Caloric	30/30	15
Rotation	15/27	12
Optokinetic	4/23	3
Optovestibular	11/23	–

y, so DP in this test was not measured. In caloric test we considered a difference in ponse from the two ears of over 20% as ication of reduced response and a limit of % was used for DP (Coats, 1969; Vesteruge & Kildegaard Larsen, 1977).

RESULTS

Ocular motor function

ontaneous, gaze and positional nystagmus. e incidence of different types of nystagmus shown in Table I. No vertical or rebound stagmus was observed among the patients.

Caloric, postrotatory, optokinetic and optotibular nystagmus. In the caloric test, all 30 patients showed reduced responses, 29 unilaterally and one bilaterally with directional preponderance in 15 cases (Table II). Maximum velocity in the postrotatory slow phase was reduced in 15 of the 27 patients tested and three of them had a bilateral impairment (Table II, Fig. 1), directional preponderance being found in 12 cases (Table II). Optokinetic tests showed reduced maximum velocities in the slow phases in 4 of the 23 patients concerned, 2 of whom had a bilateral impairment (Table II and Fig. 2). Directional preponderance was found in 3 cases (Table II). In the optovestibular tests 11 out of 23 patients had reduced maximum velocities in the slow phases (Table II, Fig. 3).

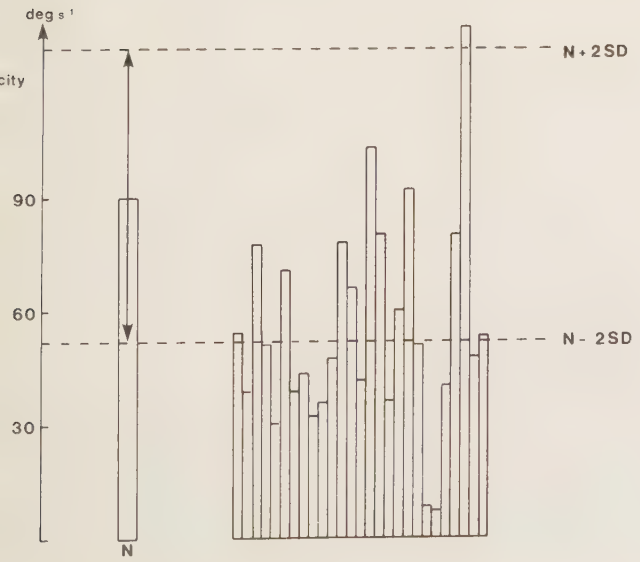

Fig. 1. Individual maximum velocity values in the slow phases of postrotatory nystagmus. Only responses in the most pathological direction are depicted. Fifteen patients have significantly slow velocities. For comparison the mean value in 20 normal subjects is depicted to the left (*N*). Dashed lines indicate a deviation of 2 SD from the mean values in 20 normal subjects.

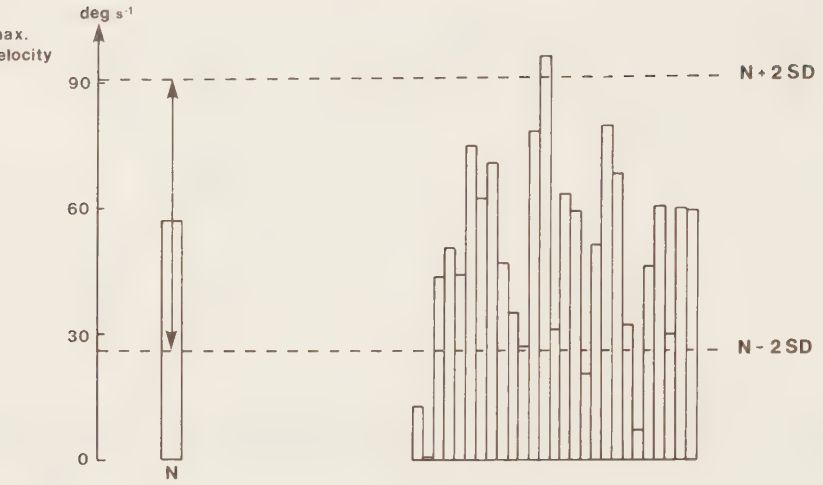

Fig. 2. Individual maximu velocity values in the slow phases of optokinetic nyst mus. Four patients have si nificantly slow velocities. Normal subjects and dashe lines as in Fig. 1.

Saccades and smooth pursuit. The peak ve- ocity in the voluntary saccades was reduced n 9 patients (Fig. 4) and normal in 21. The atients with slowed voluntary saccades had ymmetrically reduced velocities in 7 cases nd asymmetrically reduced velocities in 2 ases. There was no correlation between di- ection of spontaneous nystagmus and direc- ion of the slowed saccade.

The maximum velocity gain of smooth pur- uit (maximum eye velocity/target velocity) vas significantly reduced in 10 of the 30 pa- ients (Fig. 5), 5 of whom displayed asymmet- ic smooth pursuit with the slow pursuit in the direction of spontaneous nystagmus. Four p tients had symmetrically impaired pursu One patient without spontaneous nystagm had reduced pursuit in only one direction.

Also those patients with normal pursuit ar intensive spontaneous nystagmus (slow phas velocity more than 10 deg s^{-1}) in 50% of th cases showed a side difference in the smoo pursuit with the slowing of the pursuit propo tional to the magnitude of the spontaneo nystagmus. If there was a side difference, th pursuit was always slower in the direction the fast component of the spontaneous nysta mus. In the patients with weak nystagm

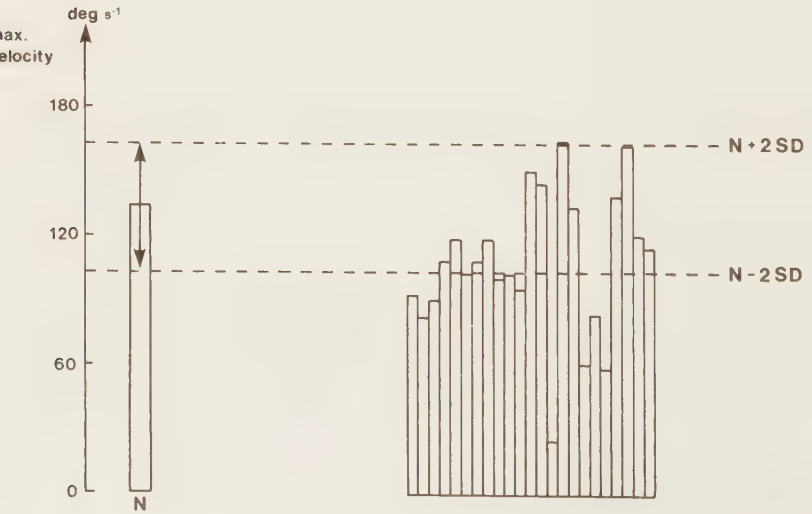

Fig. 3. Individual maxim velocity values in the slo phases of optovestibular nystagmus. Eleven patie have significantly slow v locities. Normal values a dashed lines as in Fig. 1.

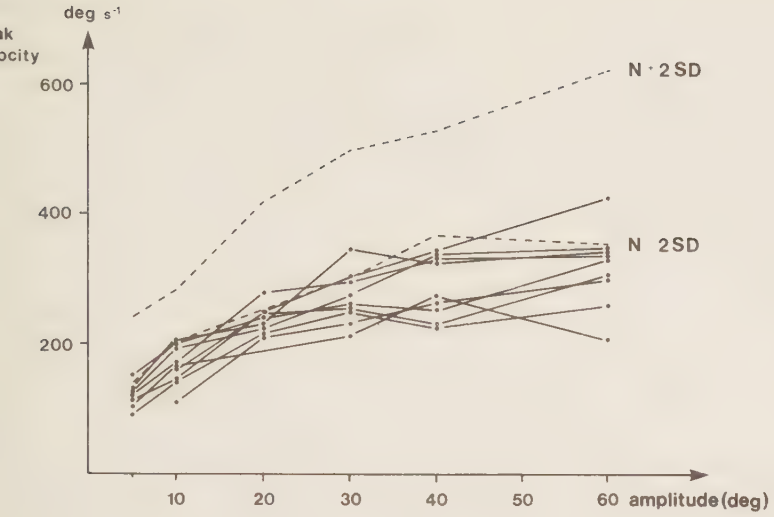

Fig. 4. Peak velocity-amplitude curves of voluntary saccades. Nine patients, those with significantly slow saccades, are depicted. The remaining 21 patients with normal saccadic velocity are not shown in the diagram. Dashed lines as in Fig. 1.

ow phase velocity less than 10 deg s^{-1}), wever, there was no correlation between e direction of slowed pursuit and the direction of nystagmus.

Neurological features

e vertigo started suddenly and was rotatory all the patients. There were no cochlear mptoms such as tinnitus or hearing loss in mbination with the vertigo. In the acute ge there were no clinical signs indicating a order of the central nervous system but during the follow-up including neurological and cerebrospinal fluid examination 'central' signs appeared in 6 cases. Thus, one of the patients had another attack of vertigo 11 months after her 'vestibular neuronitis' and this time she developed signs of brainstem involvement. In a second patient, the acute episode of vertigo was followed by signs of brainstem dysfunction during the following week. In a third patient neurological symptoms appeared gradually and a subsequent computerized axial tomography established a

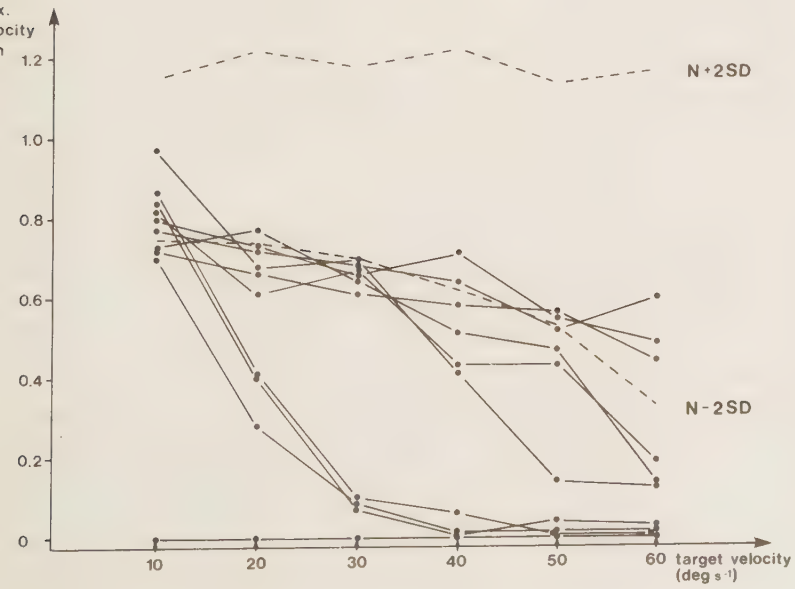

Fig. 5. Maximum velocity gain (eye velocity/target velocity) of smooth pursuit in 10 patients with significantly slow tracking are depicted. The remaining 20 patients with normal pursuit velocity gain are not shown in the diagram. Dashed lines as in Fig. 1.

Table III. *Summary of signs and symptoms which if present indicate a disorder within th central nervous system*

LP = examination of cerebrospinal fluid, C = central, P = peripheral, N = not classified

Patient ...	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	3
Neurology	+	+	+		+																									
Lp										+			+																	
Smooth pursuit	+	+	+	+	+	+				+				+	+	+														
Saccade	+	+	+	+	+		+	+	+			+																		
OKN	+	+					+				+																			
Gaze nyst.				+		+		+	+																					
Risk factor	+		+	+		+	+	+	+		+			+			+													
Conclusion	C	C	C	C	C	C	C	C	C	C	C	C	C	N	N	N	P	P	P	P	P	P	P	P	P	P	P	P	P	P

diagnosis of cerebellar hematoma. In addition a fourth patient who prior to admission had symptoms paralleling those of peripheral vestibular disease had signs of brainstem damage when neurologically examined. In 2 of the patients with vertigo as the only symptom, cerebrospinal fluid examination revealed changes compatible with those found in multiple sclerosis or infectious CNS disorders. Thus, in one case we found multiple γ-bands in liquor and in another a raised IgG/albumin ratio indicating intrathecal IgG production.

Associated disorders

As the etiologic factors behind vestibular neuronitis are not known with certainty we started to look for associated disorders (factors) among the patients (Table IV). The patients were divided into three groups, one with ocular motor abnormalities indicating a 'peripheral' cause to the vertigo, a second with 'central' ocular motor signs and a third group which could not be classified on the basis the electro-oculographic findings. With th kind of classification, vascular disease a diabetes were much more common in the 'ce tral' than in the 'peripheral' group. Convers ly, infection was more common in the 'perip eral' group than in the other two groups. (O of the patients in the 'not classified' group h two associated disorders, hypertension a diabetes.)

Neurological signs, positive findings in t cerebrospinal fluid and ocular motor abno malities indicating an intrinsic CNS disea are summarized in Table III.

DISCUSSION

The present electro-oculographic examin tions carried out on 30 patients primarily dia nosed as suffering from vestibular neuroni indicate that the disorder is not exclusive

Table IV. *Presentation of associated factors found in our cases of 'vestibular neuronitis'*

The difference between the number of associated factors in patients with electro-oculographic abnormalities interpre as 'peripheral', 'central' or 'not classified' is shown. EOG = electro-oculography, $\chi^2 = 14.95$, with 4 degrees of freed $p<0.005$

	Associated factors			
EOG	No prior illness	Preceding infection	Vascular disease	Diabetes
'Peripheral'	10	4	1	0
'Central'	2	2	5	3
'Not classified'	0	2	1	1

nited to the vestibular end organ or the pri-
ary neurons. Twelve patients showed ocular
otor abnormalities compatible with those
und in cases with intrinsic CNS disorders.
ree patients had ocular motor abnormalities
ich did not make it possible to decide
ether they were caused by a 'peripheral' or
ntral' disorder. The remaining 15 patients
d no signs of an intrinsic CNS disease when
e eye movements were analysed. The rea-
n for considering certain abnormalities in
ctro-oculography as signs of a central dys-
nction will be discussed below in detail.

Slowed smooth pursuits are known to be
mmon in various CNS disorders, such as
rtical, brainstem and cerebellar disorders
aloh et al., 1976; 1977 *a*; Sharpe et al., 1979;
ennmo & Hindfelt, 1980; Wennmo et al.,
81). Patients with peripheral vestibular dis-
ders, however, are assumed to have normal
rsuit velocity. Thus, Baloh and co-workers
976) did not find any reduction in smooth
rsuit velocity in patients with peripheral
stibular disorders, even in patients with
ontaneous nystagmus. Moreover, Sakata &
meda (1976) found that caloric nystagmus
d very little effect on eye tracking in normal
bjects and subjects with peripheral vestibu-
disorders, while the opposite was found in
tients with central vestibular disorders.

Baloh and co-workers (1977 *a*), somewhat in
ntrast to the previously mentioned study by
e same authors, reported that patients with
ute labyrinthine lesions might have tran-
ntly slowed smooth pursuit in the nystag-
c direction but that these were rapidly re-
ored by compensation mechanisms. Accord-
to this observation the pursuit abnormali-
s which were unilateral in 6 of our 10 pa-
nts with abnormal pursuit may have been
e to a peripheral vestibular disorder. Such
normalities occur, however, only if the
ontaneous nystagmus is intensive with a
w phase velocity of 10 deg s^{-1} or more,
ce lower velocities are in our material unre-
ed to side differences in pursuit.

It follows, therefore, that in the case of 3 of the 6 patients referred to above, those with slow phase velocities of 0, 4 and 9 deg s^{-1} (the borderline case with slow phase velocity of 9 deg s^{-1} also had positive liquor findings), a peripheral vestibular disorder can be excluded and the reduced pursuit velocity would seem to indicate a central disturbance. In the remaining 3 patients with unilaterally slowed pursuit a peripheral vestibular disorder cannot be excluded on the basis of the pursuit test since the slow-phase velocities were of 12, 13 and 44 deg s^{-1}.

A slowing of the voluntary saccade, found in 9 patients, is typical of disorders at the brainstem level and has not been reported in peripheral vestibular lesions (Baloh et al., 1977 *a*; Wennmo & Hindfelt, 1980; Henriksson et al., 1981).

Slowing of the velocity in the slow component in optokinetic nystagmus is also indicative of a central lesion (Carmichael et al., 1956; Jung & Kornhuber, 1964). However, some other observations suggest that a reduction in the velocity is found not only in central nervous system dysfunction, but also in acute labyrinthine lesions (Coats, 1968; Brandt et al., 1978). Such a lesion might cause either depression or enhancement of the slow phase velocity, depending on the direction and intensity of the spontaneous nystagmus. In such cases the slow phase velocity would not be reduced in both directions, as found in 2 of our patients. In the remaining 2 of our 4 patients with reduced responses the spontaneous nystagmus was rather weak, with slow phase velocities of 5 and 8 deg s^{-1}. Furthermore, one of these patients had abnormal voluntary saccades. It must therefore be concluded that the reduced velocities found in OKN in our study indicate an intrinsic CNS dysfunction.

Unilateral gaze nystagmus, found in 22 patients (Table I), may indicate a peripheral vestibular or a central nervous system disorder. Bilateral gaze nystagmus, found in 4 of our patients, is not found exclusively in CNS disorders (Coats, 1970). However, our 4 patients with bilateral gaze nystagmus also exhibited

other ocular motor abnormalities indicating an intrinsic CNS dysfunction.

Spontaneous and positional nystagmus are not diagnostic of any type of lesion (Dayal et al., 1974). Likewise, a reduction in the slow phase velocity of postrotatory or optovestibular nystagmus, if present unilaterally, is found in central as well as in peripheral lesions (Wilmot, 1973; Corvera & Romero, 1978; Wennmo & Hindfelt, 1980). The 3 patients with bilaterally reduced responses in the rotatory test also had other ocular motor abnormalities seen in central lesions.

Our interpretation that patients with symptoms typical of 'vestibular neuronitis' may have a central disturbance supports the findings of Rubenstein et al. (1980) who describe 7 patients with acute onset of vertigo resembling a peripheral labyrinthine disorder. Extended examinations revealed that these patients suffered from small cerebellar infarctions. Furthermore, several reports confirm that vertigo is the most common and sometimes the only symptom in vertebro-basilar insufficiency (Williams & Wilson, 1962; Bradshaw & McQuaid, 1963; Fisher, 1967).

In our study we found that predisposing risk factors for cerebrovascular accidents, such as vascular disease and diabetes (Baker et al., 1963; McDowell, 1967), were more common in patients with ocular motor abnormalities supporting a 'central' cause of the vertigo (Tables III, IV) than in patients with ocular motor abnormalities corresponding to a peripheral vestibular disorder.

Our results indicate that vertigo in patients with 'vestibular neuronitis' may be due to a disorder of the brainstem or cerebellum and not always to a dysfunction of the peripheral vestibular nerve.

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ZUSAMMENFASSUNG

30 Patienten, primär als Neuronitis vestibularis diagnostiziert, wurden neurootologischen, neuroophthalmologischen und neurologischen Tests unter Einbeziehung der Elektrooculographie unterzogen. Während die initiale Routineuntersuchung nicht auf Störungen ausserhalb des Nervus vestibularis hinwies, deckten die neurologische Untersuchung und die Analyse des Liquor cerebrospinalis bei 6 Patienten eine Schädigung innerhalb des Zentralnervensystems auf. Die elektro-oculographische Analyse liess bei 12 Patienten Abnormitäten erkennen, die auf eine zentrale Ursache des Schwindels hindeuteten. Bei insgesamt 13 Patienten fanden sich Zeichen einer mögliche Störung innerhalb des ZNS.

Wenn auch die Routineuntersuchung möglicherweise auf das Vorliegen einer Neuronitis vestibularis hindeutet, muss damit gerechnet werden, dass die betroffenen Patienten häufig Zeichen einer im ZNS und nicht im peripheren Nerven gelegenen Störung aufweisen.

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